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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 30 1961

AN IMMUNOLOGICAL STUDY OF COELIAC DISEASE AND IDIOPATHIC STEATORRHOEA

SEROLOGICAL REACTIONS TO GLUTEN AND MILK PROTEINS

BY

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The mechanism of the harmful action of wheat and rye gluten in coeliac disease and idiopathic steatorrhoea remains uncertain. That these proteins are responsible for the continued disability in the great majority of cases of coeliac disease was first shown by Dicke (1950). This observation was extended by Weijers and van de Kamer (1950) and first confirmed in this country by Anderson *et al.* (1952). The present theories of pathogenesis have been reviewed recently by Weijers and van de Kamer (1960) and by Frazer (1960). The more popular theory postulates that there is a congenital enzyme deficiency, with resulting incomplete digestion of gluten. Consequently a glutamine-containing polypeptide accumulates sufficiently to damage the intestinal mucosa and to cause harmful systemic effects after absorption. The second theory holds that gluten itself, or a breakdown product, acts through an immunological mechanism. The two theories are not mutually exclusive, because the postulated injurious polypeptide might behave antigenically.

French *et al.* (1957) reviewed earlier work and showed that adults with idiopathic steatorrhoea also responded to a gluten-free diet. Many patients with idiopathic steatorrhoea have histories suggesting that the disease started in childhood, and the term "adult coeliac disease" has been proposed as a better one than idiopathic steatorrhoea or non-tropical sprue (Cooke, 1958).

An obstacle to the acceptance of the immunological theory of causation has been the lack of satisfactory demonstration of antibodies to the protein concerned. We have therefore made a systematic search for antibodies to a breakdown product of gluten in the sera of patients with coeliac disease, idiopathic steatorrhoea, and other types of steatorrhoea.

As well as testing for the presence of antibodies to gluten, we have also studied the antibodies to purified milk proteins, for two reasons. First, there have been reports of clinical remissions in patients with coeliac disease after the withdrawal of milk from the diet (Kunstadter and Shultz, 1953; Breton *et al.*, 1959). Secondly, we have recently found that, compared with healthy subjects, patients with ulcerative colitis are much more likely to have antibodies at high titre to milk proteins (Taylor and Truelove, 1961).

Materials and Methods

Sera.—These were obtained from children with coeliac disease and adults suffering from various types of steatorrhoea. Control sera were taken from children at operation for tonsillectomy or circumcision, under general anaesthesia, and from healthy adults, either the staff of the Nuffield Department of Clinical Medicine or visitors to patients in a general medical ward. All sera were stored at $-20°$ C. until use.

Antigens.—The antigen used to test for antibodies to gluten was a peptic-tryptic digest of wheat gluten (fraction III) as described by Frazer *et al.* (1959). Gluten itself is insoluble in water and the usual salt solutions used in immunological procedures. Fraction III has been shown to cause clinical and biochemical relapse when fed to children with coeliac disease who have been treated with a gluten-free diet (Frazer *et al.*, 1959). Freshly prepared fraction III was used in a 1/5 dilution in phosphate-saline buffer at *p*H 6.4. It was not previously freeze-dried. The chief proteins of milk, casein, α-lactalbumin and β-lactoglobulin were used at a concentration of 0.5% in phosphate-saline buffer at *p*H 6.4. These proteins were supplied to us in a highly purified form by Dr. R. Aschaffenburg, of the National Institute for Research in Dairying, who has described the methods of preparation (Gunther *et al.*, 1960).

Tests Performed.—Sera were examined for precipitating antibodies by the gel-diffusion method of Ouchterlony (1948), using undiluted sera against fraction III. A standard complement-fixation test (Mayer *et al.*, 1948; Price, 1950) for complement-fixing antibodies to fraction III was performed. The complement-fixation test as described by Berger (1958), using alcoholic extracts of gluten and gliadin, was also attempted. The coated tanned-red-cell test (Boyden, 1951) modified by Gunther *et al.* (1960) was used with fraction III and each of the three milk proteins. The tests were read at 2 and 24 hours and the results were scored as described previously (Taylor and Truelove, 1961). The sera were tested in batches, each batch being composed of experimental and control sera. Finally all the sera from both groups were tested on a single day against the preparation of fraction III, and the results showed close agreement with the earlier batch results.

Results

Gel-diffusion Tests.—Repeated tests have been made with the sera of all the classes of patients and control subjects studied against fraction III, and the results have been uniformly negative.

Complement-fixation Tests.—No evidence of complement-fixing antibodies to fraction III has been found.

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†Nuffield Travelling Fellow.

Since positive complement fixation with alcoholic extracts of wheat gluten and gliadin by the sera of patients with coeliac disease and normal children have been reported by Berger (1958), we have repeated these tests, using a constant serum dilution of 1/4 and diluting the antigen. The results have been uniformly negative.

Coated Tanned Red Cells.—Positive results were obtained with many of the sera, which were tested in dilutions of 1/20, 1/200, 1/2,000, and 1/20,000.

Results in Children

The reactions in 24 children with coeliac disease have been compared with those in 50 children not suffering from this disease. The subjects with coeliac disease were all under the age of 15 years and consisted of children who, with one exception, had developed the symptoms of coeliac disease during the first three years of life. All suffered, or had suffered, from frank steatorrhoea as judged by biochemical tests. None had evidence of other diseases which cause steatorrhoea, such as fibrocystic disease (mucoviscidosis). In addition, all the subjects either had biopsy evidence of partial or subtotal villous atrophy of the small-intestinal mucosa (Doniach and Shiner, 1957) or had shown a favourable response to a gluten-free diet.

Reactions to Gluten Fraction III

Table I and Fig. 1 show that the spectrum of results obtained with fraction III is different in coeliac disease from that found in health, with fewer coeliac sera giving negative reactions and more giving positive reactions at higher titres (1/2,000 and 1/20,000). Although there is considerable overlap between the results in the normals and those with coeliac disease, the distributions are sharply different, with more than twice as many positive results at the higher titres in coeliac disease. In essence, therefore, patients with coeliac disease are much more likely than normal children to have circulating antibodies at high titre to fraction III.

In view of the fact that most patients diagnosed as suffering from coeliac disease are to-day treated with a gluten-free diet, which in itself might alter the serum reactions, we have analysed our material with this point in mind (Table II). Unfortunately our numbers are small, but none of the three patients on normal diet had negative or low-titre reactions (1/20) to fraction III. This is an issue which deserves further study.

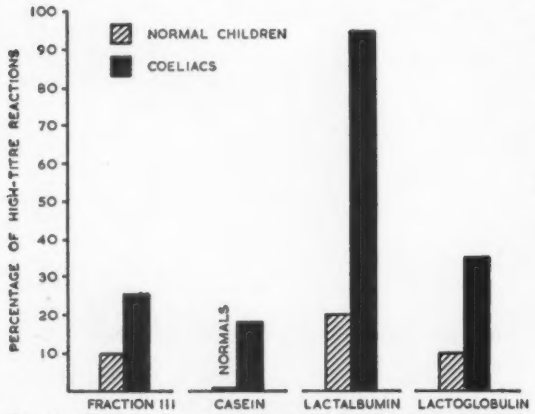

FIG. 1.—Serological reactions in coeliac disease (coated tanned-red-cell test).

TABLE II.—*Serological Reactions to Gluten Fraction III in Coeliac Disease in Relation to Gluten-free Diet*

Diet	Neg. or 1/20	1/200 and Over
Normal	0	3
Gluten-free for < 1 year	2	3
,, ,, > 1 ,, ...	6	7

Likewise, our present small numbers make it impossible to draw any firm conclusions when the serological reactions are related to the biopsy findings (Table III).

TABLE III.—*Serological Reactions to Gluten Fraction III in Coeliac Disease in Relation to Biopsy Findings*

Histological Changes in Biopsy Specimen	Neg. or 1/20	1/200 or Higher
Normal	2	0
Villous atrophy	3	9

Among the 14 patients who had biopsy performed, the two with negative biopsy findings were both on a gluten-free diet which may permit reversion of the mucosa towards normality (Anderson, 1960). Those with positive biopsy findings but negative or low-titre serological reactions to fraction III had all been on a gluten-free diet for several years.

Reactions to Milk Proteins

Table IV and Fig. 1 show the results obtained with the purified individual cow's milk proteins. Once again the sera from patients with coeliac disease show a relative scarcity of negative reactions and a relative excess of positive reactions at high titre. For each milk protein, the differences between coeliac sera and normal sera are significant statistically, although the differences are least pronounced in the case of lactoglobulin.

Independence of Reactions to Gluten Fraction III and to Milk Proteins

In view of the fact that the sera of patients with coeliac disease show more strongly positive reactions to both fraction III and milk proteins, it is of interest to know whether these reactions are related or independent of one another. Table V sets out the association between the results for fraction III and the individual milk proteins in the form of simple contingency tables. It can be seen that there is no obvious correlation, either positive or negative.

Results in Adults

The reactions in 60 cases of steatorrhoea in adults have been compared with those in 64 healthy adult subjects. The steatorrhoea patients comprised 45 examples of idiopathic steatorrhoea, seven with pancreatic steatorrhoea, and eight with post-gastrectomy steatorrhoea.

TABLE I.—*Serological Reactions to Gluten Fraction III in Coeliac Disease*

	Detailed Results						Compressed Version				Significance of Difference
	Neg.	1/20	1/200	1/2,000	1/20,000	Total	Neg. or 1/20	1/200	1/2,000 or 1/20,000	Total	
Control children ..	25	15	5	4	1	50	40 (80%)	5 (10%)	5 (10%)	50 (100%)	$\chi^2 = 13{\cdot}4$, $n = 2$, $P < 0{\cdot}01$
Coeliac disease ..	5	4	9	4	2	24	9 (37·5%)	9 (37·5%)	6 (25%)	24 (100%)	

Reactions to Gluten Fraction III

Table VI shows the results obtained with fraction III. It can be seen that the patients with idiopathic steatorrhoea have a much higher incidence of positive reactions than the normal subjects. For example, the reactions at high titre (1/2,000 or 1/20,000) are more than 10 times as frequent in idiopathic steatorrhoea as in health. The adult patients with idiopathic steatorrhoea (Fig. 2) therefore show essentially the same difference from their normal controls as do children with coeliac disease. By contrast, the patients with pancreatic steatorrhoea and post-gastrectomy steatorrhoea give results which appear to conform with those of healthy adults, although a more extensive study will be necessary to settle this point.

Reactions to Milk Proteins

When the results obtained with milk proteins are examined (Table VII) it can be seen that, as with fraction III, the patients with idiopathic steatorrhoea frequently have strongly positive reactions to these proteins and that the differences from the normal subjects are considerable and reach very high levels of statistical significance. In effect, the adult patients with idiopathic steatorrhoea resemble the children with coeliac disease in showing an excessive number of strongly positive reactions to milk proteins as well as to fraction III. By contrast, the patients with pancreatic or post-gastrectomy steatorrhoea resemble normal subjects in their reactions to milk proteins as well as to fraction III.

It should be mentioned here that the number of high-titre reactions to casein with normal adult sera is lower than that reported in a previous communication (Taylor and Truelove, 1961). This difference appears to be due to a change in technique, the use of rabbit-serum-saline as the serum diluent making the system with this antigen more stable and reducing the number of 1/2,000 and 1/20,000 reactions. The overall difference between normal and ulcerative colitis sera remains unchanged. It is interesting that this technical modification does not affect the results whether using lactalbumin or lactoglobulin.

Independence of the Reactions to Gluten Fraction III and to Milk Proteins

As in the children, the reactions to fraction III and to the milk proteins appear to be essentially independent, as can be seen from Table VIII.

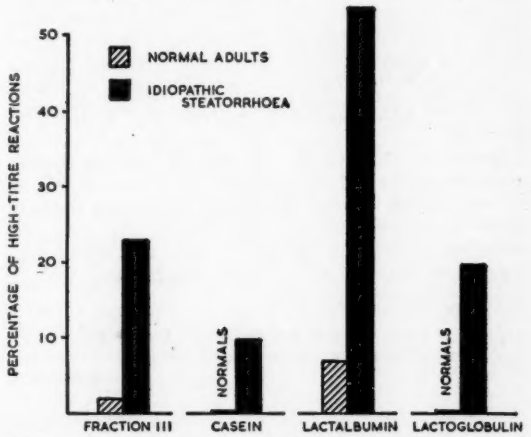

FIG. 2.—Serological reactions in idiopathic steatorrhoea in adults (coated tanned-red-cell test).

TABLE IV.—*Serological Reactions to Cow's Milk Proteins in Coeliac Disease*

Antigen	Subjects	Detailed Results						Compressed Version				Significance of Difference
		Neg.	1/20	1/200	1/2,000	1/20,000	Total	Neg. or 1/20	1/200	1/2,000 or 1/20,000	Total	
Casein	Control children ..	6	37	7	0	0	50	43 (86%)	7 (14%)	0 (0%)	50 (100%)	$\chi^2=29{\cdot}6$, n = 2, P<0·001
	Coeliac disease ..	0	3	11	3	0	17	3 (17·6%)	11 (64·7%)	3 (17·6%)	17 (100%)	
α-Lactalbumin	Control children ..	8	13	19	8	2	50	21 (42%)	19 (38%)	10 (20%)	50 (100%)	$\chi^2=29{\cdot}5$, n = 2, P<0·001
	Coeliac disease ..	0	0	1	8	8	17	0 (0%)	1 (5·9%)	16 (94·1%)	17 (100%)	
β-Lactoglobulin	Control children ..	26	11	8	4	1	50	37 (74%)	8 (16%)	5 (10%)	50 (100%)	$\chi^2=7{\cdot}4$, n = 2, P<0·05
	Coeliac disease ..	2	5	4	6	0	17	7 (41·2%)	4 (23·6%)	6 (35·2%)	17 (100%)	

TABLE V.—*Showing Lack of any Definite Association Between Serological Reactions in Coeliac Disease to Gluten Fraction III and to Individual Milk Proteins*

Gluten Fraction III	Casein				α-Lactalbumin				β-Lactoglobulin			
	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total
Neg. and 1/20	2	3	1	6	0	1	5	6	2	2	2	6
1/200	1	3	2	6	0	0	6	6	4	1	1	6
1/2,000 and 1/20,000 ..	0	5	0	5	0	0	5	5	1	1	3	5
Totals	3	11	3	17	0	1	16	17	7	4	6	17

TABLE VI.—*Serological Reactions to Gluten Fraction III in Steatorrhoea*

	Detailed Results						Compressed Version				Significance of Difference
	Neg.	1/20	1/200	1/2,000	1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	
Adult controls	45	14	4	1	0	64	59 (92·2%)	4 (6·2%)	1 (1·6%)	64 (100%)	$\chi^2=21{\cdot}0$, n = 2, P<0·001
Idiopathic steatorrhoea	14	11	10	9	1	45	25 (55·6%)	10 (22·2%)	10 (22·2%)	45 (100%)	
Pancreatic ,, ...	3	3	1	0	0	7	6	1	0	7	
Post-gastrectomy ,, ...	4	2	1	1	0	8	6	1	1	8	

Reactions to Gluten Fraction III in Relation to the Clinical Picture in Idiopathic Steatorrhoea

Age at Onset of Disease.—The patients with idiopathic steatorrhoea included a number in whom the symptoms began during childhood, a group which conforms to the conception of adult coeliac disease (Cooke, 1958). It is of interest to compare the immunological reactions of this group of cases with those of the remainder in whom idiopathic steatorrhoea appeared to develop during mature life. Table IX shows that there is no significant difference between these two groups of cases that comprise the total group of idiopathic steatorrhoea.

Small-intestinal Biopsy Findings.—Of the 45 patients with idiopathic steatorrhoea, the results of small-intestinal biopsy were available for 25. Among these 25, all except one showed villous atrophy of the mucosa. The immunological reactions in this group of patients were similar to those in the remainder in whom biopsy had not been employed as one of the diagnostic criteria.

Anaemia.—Among the 44 patients with idiopathic steatorrhoea, 34 had had anaemia as a prominent feature of their illness. These 34 subjects were more liable to show high-titre reactions to fraction III than the remainder; but the difference was not statistically significant, and more extensive observations will be necessary to decide the issue.

Gluten-free Diet.—Among the patients with idiopathic steatorrhoea there appeared to be little difference in the serological reactions of those being treated on a gluten-free diet and those on an unrestricted diet, although precise details of the diet were sometimes uncertain, so that further study is needed.

Discussion

The present study shows beyond doubt that circulating antibodies to fraction III are much more often present in high titre in patients with coeliac disease and idiopathic steatorrhoea than in healthy subjects. In addition, patients with these diseases frequently possess a high titre of antibodies to the proteins of cow's milk. Do these findings imply that gluten exerts its harmful action in these diseases by an immunological mechanism? If so, do milk proteins similarly have an aetiological role in these diseases, at any rate in some patients?

It has long been known from animal experiments that wheat gluten and gliadin can behave as antigens (Wells and Osborne, 1913). The mechanism by which, in man, ingested protein results in the formation of circulating antibodies is unknown. Anderson *et al.* (1926) have produced some evidence that infants absorb protein from cow's milk and eggs, but concluded that this absorption ceased after a few months of life. The fact that some of our control subjects had high titres of circulating antibodies to fraction III is sufficient evidence

TABLE VII.—*Serological Reactions to Cow's Milk Proteins in Steatorrhoea*

		Detailed Results						Compressed Version				Significance of Difference
		Neg.	1/20	1/200	1/2,000	1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	
Casein	Adult controls	13	29	5	0	0	47	42 (89·4%)	5 (10·6%)	0 (0%)	47 (100%)	$\chi^2=14·3$, n=2, P<0·001
	Idiopathic steatorrhoea	4	19	15	4	0	42	23 (54·8%)	15 (35·7%)	4 (9·5%)	42 (100%)	
	Pancreatic steatorrhoea	6	0	1	0	0	7	6	1	0	7	
	Post-gastrectomy steatorrhoea	4	2	1	0	0	7	6	1	0	7	
α-Lactalbumin	Adult controls	10	13	21	3	0	47	23 (48·9%)	21 (44·7%)	3 (6·4%)	47 (100%)	$\chi^2=28·3$, n=2, P>0·001
	Idiopathic steatorrhoea	1	3	16	13	9	42	4 (9·5%)	16 (38·1%)	22 (52·4%)	42 (100%)	
	Pancreatic steatorrhoea	5	0	2	0	0	7	5	2	0	7	
	Post-gastrectomy steatorrhoea	1	2	4	0	0	7	3	4	0	7	
β-Lactoglobulin	Adult controls	26	18	3	0	0	47	44 (93·6%)	3 (6·4%)	0 (0%)	47 (100%)	$\chi^2=23·9$, n=2, P<0·001
	Idiopathic steatorrhoea	10	10	14	7	1	42	20 (47·6%)	14 (33·3%)	8 (19·1%)	42 (100%)	
	Pancreatic steatorrhoea	6	0	1	0	0	7	6	1	0	7	
	Post-gastrectomy steatorrhoea	6	0	1	0	0	7	6	1	0	7	

TABLE VIII.—*Showing Lack of any Definite Association Between Serological Reactions in Idiopathic Steatorrhoea to Gluten Fraction III and to Individual Milk Proteins*

Gluten Fraction III	Casein				α-Lactalbumin				β-Lactoglobulin			
	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total
Neg. and 1/20	16	6	1	23	3	11	9	23	15	3	5	23
1/200	2	6	2	10	0	2	8	10	2	6	2	10
1/2,000 and 1/20,000	5	3	1	9	1	3	5	9	3	5	1	9
Totals	23	15	4	42	4	16	22	42	20	14	8	42

TABLE IX.—*Similarity of Serological Reactions in Idiopathic Steatorrhoea Beginning in Childhood (Adult Coeliac Disease) and in Idiopathic Steatorrhoea Beginning in Mature Life*

	Fraction III				Casein				α-Lactalbumin				β-Lactoglobulin			
	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total
Adult coeliac disease	9	5	3	17	9	5	2	16	1	6	9	16	10	4	2	16
Other idiopathic steatorrhoea	16	5	7	28	14	10	2	26	4	9	13	26	10	10	6	26

TABLE X.—*Serological Reactions to Gluten Fraction III in Ulcerative Colitis*

	Detailed Results						Compressed Version			
	Neg.	1/20	1/200	1/2,000	1/20,000	Total	Neg. and 1/20	1/200	1/2,000 and 1/20,000	Total
Adult controls	45	14	4	1	0	64	59 (92·2%)	4 (6·2%)	1 (1·6%)	64 (100%)
Ulcerative colitis	25	22	3	0	0	50	47 (94%)	3 (6%)	0 (0%)	50 (100%)

that dietary gluten can act as an antigen in apparently healthy subjects. However, we do not know whether these control subjects with high titres did not have some abnormality of the small intestinal mucosa either at the time of collection of serum or at some time in the past.

The greatly increased titres to fraction III exhibited by steatorrhoea sera might be merely an indication of enhanced absorption of unchanged, antigenic protein when the small-intestinal mucosa is diseased. However, the factor which most militates against this is that serum reactions to fraction III and milk proteins are not related in individual patients.

A further observation is that in ulcerative colitis the serological reactions to fraction III resemble those in healthy subjects (Table X), although this disease resembles idiopathic steatorrhoea in showing abnormally high numbers of high-titre reactions to milk proteins (Taylor and Truelove, 1961). The discrepancy between the behaviour in the two diseases can be best illustrated by summarizing the data as follows, in which a significant surplus of high-titre reactions compared with normal proportions is indicated by a + sign.

	Idiopathic Steatorrhoea	Ulcerative Colitis
Fraction III	+	−
Casein	+	+
Lactalbumin	+	−
Lactoglobulin	+	+

The one proviso that should be made about regarding this discrepancy as ruling out abnormal absorption as the explanation for a surplus of high-titre reactions is that proteins may vary in the ease with which they are digested, and therefore the site of mucosal damage within the gastro-intestinal tract may have an important bearing.

At least the possibility exists that the high-titre reactions in patients with steatorrhoea represent an abnormal degree of specific response to one or more dietary proteins associated with hypersensitivity of the small-intestinal mucosa to these same proteins. Testing this hypothesis requires quantitative measurement of hypersensitivity of the small-intestinal mucosa itself. Rubin *et al.* (1960) have introduced gluten into the small intestine of patients with idiopathic steatorrhoea maintained in remission on a gluten-free diet and have shown that lesions typical of the disease appeared in the previously histologically normal mucosa of the proximal ileum. This elegant study may provide a valuable technique for future investigations of this problem.

Studies of circulating antibodies to dietary proteins may also prove to be of importance in the diagnosis and treatment of various enteropathies. For example, it is well known that some patients with idiopathic steatorrhoea fail to show any beneficial response when gluten is excluded from the diet. We have recently seen one such patient whose jejunal biopsy showed subtotal villous atrophy. Reaction of her serum to fraction III was negative. In such subjects it would be of interest to determine levels of circulating antibodies to other food proteins, such as those of milk, and then to determine by exclusion diets whether any favourable result obtained was related to the level of circulating antibodies.

ADDENDUM.—The serum of the patient just mentioned was found to give high-titre reactions to cow's milk proteins. She was treated with a milk-free diet (but one containing gluten) and has shown an excellent clinical response during the two months that have elapsed. More prolonged observation of this patient, as well as studies of other patients, will be necessary before it is possible to conclude with certainty that milk can play a decisive part in some patients with idiopathic steatorrhoea or coeliac disease.

Summary

Sera of patients with coeliac disease and idiopathic steatorrhoea contain antibodies to a proteolysed fraction of wheat gluten in significantly higher incidence and titre than the sera of control subjects. This is also true for purified cow's milk, casein, α-lactalbumin, and β-lactoglobulin. These findings are discussed in relation to aetiology and treatment of coeliac disease and idiopathic steatorrhoea.

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CLINICAL PATTERNS AND COURSE OF ANAEMIAS IN GENERAL PRACTICE

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Anaemia is an important clinical condition in general practice for three very good resons: (1) it is frequent —according to French and Israëls (1955) an average G.P. may expect to meet 40–50 new cases each year; (2) it is the cause of much "sub-health"; and (3) it is eminently controllable. However, in spite of this importance it is probable that many anaemic patients remain undiagnosed and ineffectively treated.

The family doctor should play an important part in the control of anaemia. Obviously he must be constantly on the look-out for new cases, and must have readily available laboratory facilities to confirm his clinical suspicions. Having made the diagnosis, he must then plan and carry out long-term treatment and observation to ensure complete correction of the anaemia.

How far these ideals apply in actual practice is not known because of lack of any reliable information. Apart from the work of enthusiasts such as French (1948, 1953), French and Israëls (1955), and Semmence (1959), there are few reliable reports on anaemia in general practice.

Present Investigation

Because of the lack of such information this study was planned to review cases of anaemia in a general practice during a period of 10 years (1950–60).

The objects of the study were: (1) to collect cases for five years (1950–5) and then to follow them up for another five to ten years; (2) to estimate the incidence of anaemia in a general practice; (3) to define the common clinical types of anaemia; (4) to discuss the management, including the scope of a family doctor who has full diagnostic facilities available; and (5) to describe the course of the disease and the situation of the patients after five to ten years.

The practice is situated in a middle-class suburb in south London and its average size during the period 1950–5 is as shown in Table I.

TABLE I.—*Average Population at Risk* (1950-5)

Age:	0–	10–	20–	30–	40–	50–	60–	70+	Total
Males	405	246	349	380	398	302	173	127	2,380
Females	379	351	350	397	403	322	218	142	2,562

Diagnostic Facilities and Criteria

In this area all the family doctors have full and complete access to the pathological and radiological departments of the local hospitals. After a pilot study it was decided to restrict the types of cases to be studied to those in which "anaemia" presented as the main clinical feature. The decision to investigate the patient was based on clinical judgment. Pallor, debility, and shortness of breath were the most frequent reasons. Although the results cannot by reason of such clinical assessments give a true incidence of anaemia in practice, it must be appreciated that it is in just this way that medicine is practised and that it is not really practicable to carry out routine investigations on every patient seen.

Excluded from this review and follow-up were (*a*) those cases of anaemia that were picked up incidentally through routine blood tests during pregnancy (these cases were excluded because subsequent follow-up was difficult), and (*b*) those in which anaemia developed during the later stages of already established diseases.

"Anaemia" was regarded as being present when the level of haemoglobin reported was below 80% (100% = 14.8 g./100 ml.). Since only the one hospital laboratory was used during this study there was no variation in technique to be accounted for. Screening tests were not carried out; the patient was referred to the laboratory when anaemia was suspected, and the haemoglobin level, red-cell count, and erythrocyte sedimentation rate were estimated.

Methods

The methods of recording were simple. As each new case was diagnosed a card was made out and clinical details and haematological findings were recorded. These cards were then filed in small card-index boxes. The patients were all seen fairly regularly. Since the average yearly attendance rate in this practice was between three and four attendances per patient per annum no special reminders were necessary for patients to reattend. During the years 1950–60, five to ten years from the beginning of the study, those patients who were still in the practice were seen and re-examined.

Results

Incidence.—During the period of "collection" (1950–5) 222 patients (44 males, 178 females) were seen with anaemia as the main clinical feature. Records were also kept of the other clinical types of anaemia that occurred in the practice during this same time, and these amounted to 164 anaemias diagnosed during pregnancy by routine blood test, and 47 anaemias occurring in the later stages of other diseases (males 20, females 27). The incidence of *all* types of anaemia over the five years was therefore 433 cases (8.7%), and the *annual incidence was approximately 17.5 per 1,000.* This means that the average family doctor with a list of 2,500 may expect to meet some 52 patients with anaemia each year, a figure very close to that of French and Israëls (1955). It is of some interest to observe that on average about 100 patients are referred for haematological investigations each year, so that anaemia was present in some 86% of those investigated. For reasons already given only those patients who presented anaemia as the main clinical feature were followed up, and it is this group only that is discussed.

Age-and-Sex Distribution.—There was a fourfold predominance of females. The age-and-sex distribution is given in Table II. The sex differences of anaemia are well known, but the differing age distributions in the two sexes are less so. In males anaemia was most frequent in boys under 10 and in men over 50. The incidence of anaemia in these young boys was higher even than that in girls—the only period in which this was the case. In females the pattern was rather

TABLE II.—*Age-and-Sex Distribution of* 222 *Patients with Anaemia*

Age:	0–	10–	20–	30–	40–	50–	60–	70+	Total
Males	14	2	—	2	2	10	5	9	44
Females	7	9	26	36	46	22	19	13	178
				Rate per 1,000					
Males	35	8	—	5	5	33	29	71	
Females	20	26	74	90	115	68	87	91	

different. The peak occurred in the fifth decade, but the rates were high from the age of 20 onwards. This was probably connected with the menstrual blood loss during the reproductive phase.

Clinical Types

Two main types of anaemia were differentiated—hyperchromic and hypochromic (iron-deficiency). The hypochromic anaemia cases (with the colour index below 1) were further subdivided clinically into those where subsequent investigation revealed a definite underlying cause for the anaemia and those in which no obvious cause was evident. The distribution of these groups is shown in Table III. A number of interesting facts emerge from these distributions.

If we distinguish the two subgroups of hypochromic anaemias—that is, those with and those without obvious underlying disease—their proportions in males and females were very different. In 46% of the males no obvious underlying disease was discovered, whereas this group accounted for 83% of the females. The numbers in the various age-groups were very different. In males it was in infancy and early childhood that most of these cases of hypochromic anaemia were found. These anaemic boys accounted for 70% of this type of anaemia. It is very likely that nutritional deficiencies were the cause. In females the peak age-periods were at 30–49—that is, in the later reproductive phase—and the cause here must have been the negative iron balance from excessive menstrual blood loss.

The underlying conditions causing hypochromic anaemia included direct bleeding from a peptic ulcer in eight and hypochromic anaemia some years after a gastrectomy in a further seven. Other prominent conditions were new growths, usually in either the stomach or the colon, and rheumatoid arthritis; these accounted for a further 14 patients.

Since subclinical gastric haemorrhage has been shown to occur with aspirin tablets a note was made of the patients who were in the habit of consuming aspirin regularly. These amounted to 22 in all, 10 women and 1 man in the group with no obvious underlying disease, and in 11 patients (7 women and 4 men) with obvious underlying disease—that is, new growths, myeloma, and rheumatoid arthritis.

During the five-year period 14 patients were under treatment for pernicious anaemia. This represents a rate of 2.8 per 1,000, which is much higher than the national average of 1.3 quoted by Scott (1960).

Comment.—It is quite clear that in general practice hypochromic anaemias, associated with iron-deficiency, of one cause or another, are by far the most common types. Of the 222 cases, 205 (92%) were of iron-deficiency anaemia, and only 14 (7%) of pernicious anaemia and 3 (1%) of haemolytic anaemia. Considering the many varied conditions that were associated with the anaemia, it is important to realize that "anaemia" of itself was no definitive diagnosis. It was merely a sign and the result of some defect in blood formation, loss, or obstruction. In each case a careful clinical assessment and a search for the cause had to be made.

Severity

It was surprising how human beings could go about their daily tasks with anaemias of great severity. Of the 222 cases, 41 (18%) had initial haemoglobin levels below 50% (Table IV), and five (2%) had levels below 30%.

TABLE IV.—*Distribution of 41 Cases with Initial Haemoglobin Below 50%*

	Hypochromic		Hyperchromic		Total
	No Obvious Cause	Underlying Disease	P.A.	Haemolytic	
Males ..	2	4	1	1	8
Females ..	15	14	3	1	33

Management

Diagnosis.—As a first step in management the correct diagnosis had to be made, for, as already stated, "anaemia" was of itself an inadequate label. When the haemoglobin was below the critical level of say 80%, a search had next to be made for the cause and type of the anaemia. Co-operation with the haematologist will help to define the type, but a careful clinical assessment is required, especially when dealing with hypochromic anaemia, to discover any underlying disease. For this purpose a clinical examination, including rectal and pelvic examinations, followed by radiographs of the digestive tracts and tests for occult blood in the faeces may be required.

Referral to Consultant.—In this practice, with full access to all pathological and radiological examinations, only 18 out of the 222 patients reviewed, or 8% of the total, had to be referred to a consultant physician for elucidation of the anaemia and advice on its management. Of course, others were referred for treatment of their underlying disease—for example, new growths and peptic ulcers—after the exact diagnosis had been made. The fact that in this particular practice 92% of anaemias were diagnosed and elucidated by the family doctor without the aid of a consultant physician, but

TABLE III.—*Distribution of Types of Anaemia*

	Males									Females								
Age:	0–	10–	20–	30–	40–	50–	60–	70+	Total	0–	10–	20–	30–	40–	50–	60–	70+	Total
Hypochromic:																		
No obvious cause ..	14	2	—	—	—	2	2	—	20 (46%)	7	8	25	33	42	18	7	6	146 (83%)
Underlying disease ..									17 (38%)									22 (12%)
Peptic ulcer	—	—	—	—	—	1	2	1	4	—	—	—	1	1	—	2	—	4
Post-gastrectomy ..	—	—	—	1	1	2	—	1	5	—	—	—	—	—	1	1	—	2
Hiatus hernia	—	—	—	—	—	—	—	1	1	—	—	—	—	—	—	2	—	2
New growth	—	—	—	—	—	—	1	2	3	—	—	—	1	—	—	2	3	6
Leukaemia	—	—	—	1	—	1	—	—	2	—	—	—	—	—	—	1	—	1
Myeloma	—	—	—	—	—	—	—	1	1	—	—	—	—	—	1	—	1	2
Rheumatoid arthritis ..	—	—	—	—	1	—	—	—	1	—	—	—	—	2	2	—	—	4
Chronic nephritis ..	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	1
Hyperchromic:																		
Pernicious anaemia ..	—	—	—	—	—	4	—	1	5 (11%)	—	—	—	1	1	—	4	3	9 (4%)
Haemolytic ,, ..	—	—	—	—	—	—	—	2	2 (5%)	—	—	1	—	—	—	—	—	1 (1%)
Total	14	2	—	2	2	10	5	9	44 (100%)	7	9	26	36	46	22	19	13	178 (100%)

with the full co-operation and support of the local hospital diagnostic services, shows that the control of anaemia in the community is essentially a matter for the family doctor, provided he has the diagnostic facilities at his disposal. The 18 referred to a consultant physician were six males—two each with hyperchromic anaemia, leukaemia, and haemolytic anaemia; and 12 females—three with hyperchromic anaemia, two each with hiatus hernia and new growths, and one each with rheumatoid arthritis, chronic nephritis, myeloma, hypochromic anaemia, and haemolytic anaemia. The severity of the anaemia was not in itself a primary factor in deciding whether the patient was to be referred to a consultant. In fact, three of the five patients with haemoglobin levels below 30% were managed at home.

Treatment

The treatment naturally depended on the type and cause of the anaemia. Underlying disease required treatment—for example, peptic ulcer, new growth, etc.—but even here correction of the anaemia was an urgent primary matter. No patients treated at home were thought to require blood transfusions, although some of those admitted to hospital for elective treatment of underlying disease did receive blood as part of their management.

Hypochromic anaemia was treated with iron. Oral iron in the form of the standard ferrous sulphate preparations was given in the first instance where the haemoglobin was between 50 and 80%, and where the haemoglobin level was below 50% additional intramuscular iron ("imferon") was used on occasion. It is of interest to note that the intolerance rate of ferrous sulphate was as high as 20%. Most of these patients, however, were able to tolerate the gluconate or fumarate compounds. Follow-up was maintained for as long as possible with regular blood checks, but once patients felt better many were loath to continue to attend over the years, and no special efforts were made to pick up the defaulters until the results of the study were known.

Hyperchromic anaemia cases had first to be accurately diagnosed by gastric analyses and marrow examination. Since all but three of these were pernicious anaemia the management was relatively simple, with regular vitamin B_{12} injections. Follow-up with regular three-monthly blood checks was easily maintained in this group because the patients had to attend for injections.

Course and Follow-up

Patients still in the practice in 1959–60 (5–10 years from beginning the study) were seen, examined, and their haemoglobin levels estimated. During the follow-up period 15 patients (7%) (3 males and 12 females) had moved out of the practice. A further 18 had died from the following: males—new growths (3), leukaemia (2), myeloma (1), haemolytic anaemia (1), and one man with a gastric ulcer who died from a cerebral haemorrhage; females—new growths (6), myeloma (2), chronic nephritis (1), and rheumatoid arthritis (1).

There were therefore 189 patients who were reassessed in 1959–60. Analysis of the haemoglobin figures at follow-up showed that anaemia (Hb below 80%) was still present in 61 (32%). The distribution of these patients is shown in Table V. It was far from satisfactory to find that at follow-up one-third of the patients were still anaemic. Who were they? Why were they still anaemic? What should be done about this situation?

Who were they?—Patients with hypochromic anaemia with no major underlying disease accounted for 55 out of the 61, and 50 of these were females. Women aged between 30 and 60 were most liable to relapse, but three out of the five males who relapsed were children. The hyperchromic anaemias presented few problems. Those who relapsed were two patients with haemolytic anaemia whose course is known to fluctuate and one old woman with pernicious anaemia who required iron and folic acid to maintain her haemoglobin level at over 90%.

Why were they anaemic?—All the patients with hypochromic anaemia who relapsed had either stopped taking oral iron or were women who were having very heavy menstrual losses and in whom there was a negative iron balance in spite of their taking iron.

What should be done?—Patients with hypochromic iron-deficiency anaemia, by far the most common type of anaemia in the community, should be under constant medical supervision with regular haemoglobin estimations, and they should be seen at regular intervals to ensure that they continue to take the iron that is so necessary for the control of their anaemia. They should be seen at least two or three times a year to check their haemoglobin levels.

When can treatment be stopped safely in iron-deficiency anaemias?—This is an individual matter in each case. As a general rule it is unwise to stop therapy until well after the menopause in women with hypochromic anaemias. Where underlying diseases have been cured treatment can cease once normal haemoglobin levels have been maintained for over a year. However, all patients who have been on treatment should have haemoglobin estimations after six months of ceasing iron therapy to make sure that all is still well.

Discussion

The importance of "anaemia" as a frequent cause of "sub-health" has already been referred to in a general way. The subject can now be discussed in relation to the findings of this study. The estimated annual incidence of all forms of anaemia was 17.5 per 1,000. This is a high figure, representing about one new case to be diagnosed and managed each week of the year in an average-sized British practice. The family doctor has therefore to be alive to the condition and be given opportunities for early diagnosis and encouragement in supervision of his patients. Unless this awareness is present and these facilities are available the diagnosis will not be made and many patients will suffer unnecessarily.

TABLE V.—*Patients with Haemoglobin Level of Less than 80% at Follow-up*

	Males									Females								
Age:	0–	10–	20–	30–	40–	50–	60–	70+	Total	0–	10–	20–	30–	40–	50–	60–	70+	Total
Hypochromic:																		
No obvious cause ..	3	1	—	—	—	—	1	—	5/17 (30%)	1	2	5	12	14	11	2	3	50/138 (36%)
Underlying disease ..	—	—	—	—	—	—	—	2	2/12 (17%)	—	—	—	—	—	1	—	—	1/11 (9%)
Hyperchromic	—	—	—	—	—	—	—	1	1/4 (25%)	—	—	—	1	—	—	—	1	2/7 (29%)

As with many other conditions, hospital experiences cannot be applied to general practice. The types of anaemia seen most often in the community, and therefore in general practice, have quite a different slant and pattern from those seen in hospital.

In this series of 222 patients who presented clinically with anaemia as the major feature, hypochromic anaemia accounted for 92% and hyperchromic anaemia for 8%.

In 17% the hypochromic anaemia was found to be the result of some obvious underlying disease; in 75% there was no very obvious cause for the hypochromic anaemia, but it was probably the result of excessive blood loss—for example, menstrual—and inadequate nutrition.

The importance of hypochromic anaemia in pregnancy must also be remembered. Although this type was not specially studied here, during the five years 167 expectant mothers were found to have a haemoglobin level below 80% (out of nearly 400 deliveries in the practice during this time), a rate of 42%. Giles and Burton (1960), in Stoke, reported a rate of 66%.

The most vulnerable groups of patients were women from 30 upwards, young male infants, and old men. This liability of male infants to iron-deficiency anaemia is interesting in that it fits in with the generally excessive morbidity of male children. The vulnerability of the women in the 30–60 period was undoubtedly related to the negative iron balance from excessive menstrual losses. In the elderly of both sexes the anaemias were much more likely to be associated with some underlying diseases.

Hyperchromic anaemia was most frequent in those over 50. No case of hyperchromic anaemia occurred during pregnancy.

Reference has been made to the amazing tolerance and adaptive powers of the human body in regard to anaemia. During this study 41 patients (18%) had a haemoglobin of less than 50% at the time of diagnosis. In 5 (2%) the initial level was between 20 and 30%, and yet these patients were able, with difficulty admittedly, to carry on their daily tasks. This is also a reflection of the delay of the diagnosis. The blame for this delay was very often the patient's, because the diagnosis was usually made by the doctor at the first consultation.

The management of these anaemic patients must follow a definite pattern in order to be successful. A confirmatory blood examination is necessary to make the diagnosis of "anaemia." This, however, is merely the beginning. The patient has next to be clinically examined to exclude or discover any underlying disease. Further investigations, both radiological and pathological, may also be required before the type of anaemia and its cause can be ascertained. Given the facilities for investigation, the family doctor should be able to assess most of his anaemic patients.

Treatment should be kept as simple as possible, and stress must be laid on the necessity for long-term supervision. The importance of such supervision is evident from an examination of the results of reassessment at the end of 5 to 10 years. In one-third (32%) anaemia was still present. The results were particularly poor in women aged 30 to 60 with hypochromic anaemia. In view of these unsatisfactory results certain conclusions and recommendations can be made.

Conclusions

Hospital pathological laboratories and x-ray departments should be open to all local family doctors. Unless they are it is impossible for the family doctor to diagnose anaemia early, and difficult to supervise and maintain satisfactory treatment.

It is important to make students and doctors aware of the high frequency of the common types of anaemia and of the principles of management.

In management the most important points are: the need for an accurate initial diagnosis, particular care being taken to exclude any underlying disease as the cause of the anaemia; to appreciate that satisfactory results can be obtained by very simple treatment; and to realize that long-term supervision of the patient must be maintained with regular haemoglobin estimations extending over many years. If this supervision is neglected the tendency for relapse is great.

Summary

Anaemia is a very important illness in our community because of its high prevalence and the ill-health that it causes; it is so easily remedied.

A study is reported from a London general practice of 5,000 patients. Full facilities are available in the area for family doctors to investigate their patients. Cases of anaemia were recorded to assess the incidence, the distribution of the common varieties, and the level of haemoglobin at the end of 5 to 10 years.

"Anaemia" was regarded as being present when the haemoglobin level was below 80%. Only those cases where the anaemia was the chief presenting clinical feature were studied. There were 222 of these in five years (1950–5). Excluded were 164 women in whom the anaemia was diagnosed incidentally during pregnancy, and 47 patients in whom anaemia developed during the later stages of other diseases.

The total incidence rate (including all cases and types) of anaemia worked out at 17.5 per 1,000 per annum.

There was a 4:1 female predominance (178 females and 44 males) of anaemia. The most vulnerable age periods were: in males, children under 10 and men over 60; and in women, all age-groups over 30, with a peak at 50–59.

Hypochromic anaemias (iron-deficiency) accounted for 92% (205 patients) of all types. In 17% (39) of these an obvious underlying disease was present at the time the diagnosis was first made. In the other 83% (166) cases of hypochromic anaemia no serious underlying disease was detected. The proportion of cases with underlying disease was much higher in males (54%) than in females (17%), and in the elderly of both sexes. Pernicious anaemia was present in 14 patients—a rate of 2.8 per 1,000.

Many patients were severely anaemic when first diagnosed. In 41 (18%) the initial haemoglobin level was below 50% and in 5 (2%) it was below 30%.

With the full diagnostic facilities 92% of these patients had their anaemias investigated, diagnosed, and managed by the family doctor alone.

The routine treatment in hypochromic anaemias was oral iron. (There was a 20% intolerance rate to ferrous sulphate.)

At the end of 5 to 10 years, in 1959–60, there were 189 patients still in the practice (15 had moved and 18

had died), and these were all reassessed. In 61 (32%) the haemoglobin level was below 80%. Hypochromic anaemias, of the non-specific variety, accounted for 55 (50 in females). The reasons for these relapses were generally failure to continue with iron therapy.

As a result of this study it is recommended that full facilities for investigations be given to all family doctors in at least one hospital in each local hospital group; that more teaching be given to undergraduates and post-graduates (in general practice) on the frequency of anaemia and on the principles of successful management; and that the importance of the long-term treatment and follow-up of the particularly vulnerable group of women in their later reproductive phase (that is, 30–50) is appreciated. It is quite useless to treat those women by a prescription for 100 iron tablets and then to forget all about them. Treatment, with regular blood tests, is necessary right up to and well past the menopause.

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PREVALENCE OF ANAEMIA IN THE GENERAL POPULATION

A RURAL AND AN INDUSTRIAL AREA COMPARED

BY

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The results of a study of the prevalence of anaemia in an industrial community, the Rhondda Fach, have already been published (Kilpatrick and Hardisty, 1961), and in the present paper the findings are given of a survey carried out for comparative purposes in a rural area, Wensleydale, the largest of the Yorkshire dales.

The inhabitants of Wensleydale had previously been the subject of epidemiological studies by Dr. Pickles, of Aysgarth, and the decision to sample this population was made easy by a fortunate coincidence: Dr. J. S. Lawrence and his colleagues of the Empire Rheumatism Council Field Research Unit had elected to go there to study rheumatic conditions in an agricultural community, and it was decided to join them to determine the prevalence of anaemia in their sample.

Sample and Methods

Wensleydale is about 35 miles (56 km.) long, and the size of the valley with its scattered population (about 0.04 person per acre) made it impracticable to work on a random sample of the whole population; a representative area was therefore selected. After a private census had been made it was decided to study the population of both sexes, aged 15 and over, in the southern half of the village of Hawes, in three of the near-by hamlets, and in about 40 square miles (103 sq. km.) of the surrounding farming area in the upper end of the dale. Because of the knowledge of the structure of the population in this area it is thought that the subjects studied were a fair but perhaps not an impeccable sample of the population as a whole. The total available population was 547, of whom 412 (75%) were examined. This survey was planned for August and September, 1958, in the hope that the hay harvest would be completed before then, but because of bad weather the harvest was late, and the response rate was therefore lower than in the previous survey. The numbers included in the survey are shown in Table I.

Our base was in the centre of Hawes, where the Manchester University Survey van and trailer provided an almost self-contained unit in which some 30 people were seen each day. Because it was impossible to have full facilities in the van for blood-counting, and so that the findings of this survey would be comparable to the previous studies, the blood taken by venepuncture during one day was each evening taken by road to Kendal and put on the night train so that the samples arrived at the laboratory in Cardiff Royal Infirmary the next morning. The specimens were then examined in exactly the same way as during the Rhondda survey (Kilpatrick and Hardisty, 1961). The arbitrary levels of haemoglobin chosen for "anaemia" were the same—12.5 g./100 ml. (85%) or less for men and 12 g./100 ml. (81%) or less for women.

TABLE I.—*Details of Population Studied*

Age-group	Men		Women	
	No. Living in Area	No. Examined	No. Living in Area	No. Examined
15–24	53	29 (55%)	45	32 (71%)
25–34	37	26 (70%)	51	40 (78%)
35–44	54	34 (63%)	52	45 (86%)
45–54	48	36 (75%)	42	34 (81%)
55–64	33	25 (76%)	38	32 (84%)
65–74	27	20 (74%)	37	33 (89%)
75+	13	12 (92%)	17	14 (82%)
	265	182 (69%)	282	230 (82%)

Because this survey was planned purely as a prevalence study no further investigation or treatment was done, but the name of each person found to be anaemic was immediately sent to the general practitioner concerned.

Results

In men the mean level of each index, except P.C.V., declines fairly steadily with age; there is no fall in P.C.V. until the 55–64 year age-group, but the means thereafter are much lower (Table II). The scatter of values of each index, as measured by the standard deviation, shows a tendency to increase with age, except in the case of the serum iron. This is almost certainly a reflection of an increased proportion of subjects with low values in the higher age-groups.

In women the levels for all indices are lower than those for men, though the differences are much less marked over the age of 65 years (Table II). There is no downward trend of values with increasing age, and

the scatter of values, as measured by the standard deviation, is less evident.

Comparison with the Rhondda data is possible only in men aged 35–64 years and in women aged 55–64. Table III shows the comparison of means and standard errors between Wensleydale men and Rhondda men

TABLE II.—*Haematological Indices. Means and Standard Deviations*

Age	Hb (g./100 ml.)		P.C.V. (%)		M.C.H.C. (%)		Serum Iron (μg./100 ml.)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Men								
15–24	14·07	0·81	44·33	2·88	31·76	0·79	142·24	47·79
25–34	14·31	0·95	45·23	3·45	31·62	0·94	115·27	47·27
35–44	14·32	0·94	45·03	2·60	31·79	1·32	129·94	60·19
45–54	14·10	1·11	44·83	3·93	31·56	2·30	126·08	95·36
55–64	13·90	1·24	45·10	3·67	30·76	1·13	105·44	44·11
65–74	13·15	2·07	42·95	5·35	30·60	1·96	97·06	43·18
75+	13·28	1·52	43·67	4·81	30·42	1·31	92·50	46·53
Women								
15–24	11·87	1·96	38·59	4·82	30·63	2·18	97·19	44·44
25–34	12·65	1·17	40·43	3·42	31·28	1·55	92·92	38·25
35–44	12·68	1·30	40·92	3·48	30·98	1·36	107·89	22·67
45–54	13·12	1·02	42·10	3·35	31·12	1·15	98·09	30·01
55–64	13·02	1·14	41·70	3·63	31·28	1·22	99·19	40·05
65–74	13·02	1·10	41·68	3·47	31·30	1·05	108·41	38·06
75+	12·85	1·32	42·50	4·92	30·36	1·55	91·00	44·05

TABLE III.—*Comparison of Haematological Indices*

	Hb (g./100 ml.)	P.C.V. (%)	M.C.H.C. (%)	Serum Iron (μg./100 ml.)
Men aged 35–64 Years				
Wensleydale ..	14·13±0·12	44·94±0·34	31·43±0·14	121·95± 5·17
Rhondda miners and ex-miners	14·59±0·07	45·60±0·20	32·33±0·08	119·02± 3·02
Rhondda non-miners ..	14·73±0·07	45·59±0·21	32·58±0·09	123·81± 3·11
Women (55–64 Years)				
Wensleydale ..	13·02±1·14	41·70±3·63	31·28±1·22	99·19± 7·07
Rhondda ..	13·31±1·65	41·69±4·28	31·67±1·69	103·80± 3·47

(miners and ex-miners and non-miners) in the age range 35–64 years. So far as haemoglobin, P.C.V., and M.C.H.C. are concerned the figures found in Wensleydale are significantly lower than those from the Rhondda.

A comparison of the Rhondda and Wensleydale women aged 55–64 years is also given (Table III). As in the comparison of the men the figures for the women of Wensleydale are again lower than those of the Rhondda women.

Cases of Anaemia

The prevalence of anaemia in the various age-groups is given in summary in Table IV. Anaemia, though uncommon, is to be found in young males; it is found more often as age advances. In women, anaemia is much more common at all ages—strikingly so in fact during the child-bearing years. From 65 years onwards the prevalence of anaemia is similar in men and women. In both sexes at all ages almost all anaemia can be attributed to iron deficiency (Table V); we have, however, no information about how this occurs.

Discussion

Two findings stand out from the results of this survey. The first is the strikingly high prevalence of anaemia in women of all ages; the second is that, contrary to what might have been expected, the haematological indices are lower in those people living in an agricultural area than in an industrial one. The explanation for the second finding is unknown and would not be easy to discover without extensive sociological investigation. It is probable, however, that diet is a contributory factor, because much of the produce of the relatively small farms in the area is marketed rather than consumed locally.

The finding that as many as 25–30% of females aged 15–34 years are anaemic is surprising, but menstruation and child-bearing probably account for most of the anaemia discovered. There is therefore a strong case for more frequent haemoglobin estimations in women and perhaps the more liberal use of iron, as most of the anaemia is of the iron-deficiency type. Iron-deficiency anaemia in young men is uncommon, but our findings, together with those of the M.R.C. (1945), Shorthouse and King (1951), Leonard (1954), Stewart *et al.* (1957), and Brumfitt (1960), show clearly that it does occur.

About 12% of women in Wensleydale between 55 and 64 years were anaemic—this is in close agreement with the 13.9% found for the women of the Rhondda examined previously. Over the age of 65, however, the prevalence of anaemia in both sexes rose again in Wensleydale to more than 20% of those examined. The finding of so much iron-deficiency anaemia in the older age-groups is at variance with many standard textbooks, but recently other authors have also commented on its prevalence (Lange and Skjaeggestad, 1958; Bedford and Wollner, 1958; Semmence, 1959).

While it is probable that a proportion of the anaemia in older women is the end-result of a chronic anaemic state which starts during the child-bearing years, some additional factor must be involved to explain the increase in its prevalence after the age of 65 years; and

TABLE IV.—*Prevalence of Anaemia*

Age-group	Men		Women	
	No. Examined	No. Anaemic	No. Examined	No. Anaemic
15–24	29	1 (3·4%)	32	9 (28·0%)
25–34	26	0 (0·0%)	40	10 (25·0%)
35–44	34	1 (2·9%)	45	11 (24·0%)
45–54	36	3 (8·3%)	34	4 (12·0%)
55–64	25	2 (8·0%)	32	4 (12·5%)
65–74	20	4 (20·0%)	33	7 (21·0%)
75+	12	3 (25·0%)	14	3 (21·0%)
	182	14	230	48

TABLE V.—*Type of Anaemia*

	Men	Women
Undoubtedly hypochromic (M.C.H.C. 30% or less)	11	31
Borderline (M.C.H.C. 31%)	1	12
Normochromic	2	5
Total	14	48

probably this same factor accounts for the anaemia found in the older men. There is much evidence that the factor is blood loss, and anaemia in the elderly should always be carefully investigated with this in mind; but it is quite possible that other factors, such as dietary insufficiency, may also play a part in its causation.

Summary

A survey to determine the prevalence of anaemia in an agricultural community, Wensleydale, was carried out in August, 1958. A sample of men and women aged 15 and over was examined and a comparison made with

the results of a previous survey in an industrial community, the Rhondda Fach. In comparable age-groups the mean values for haemoglobin, P.C.V., and M.C.H.C. were significantly lower in Wensleydale than in the Rhondda.

In Wensleydale the prevalence of anaemia in males aged 15–24 was 3.4%, falling to zero in those aged 25–34 and then rising in later decades to 25% in the one 75 years and over. In females of 15–24 years the prevalence of anaemia was 28%. This figure fell to 12% in age-group 55–64 years and subsequently rose to 21% in the later age-groups. Most of the anaemia was of the iron-deficiency type.

Many people contributed to the success of this survey, which was carried out during the tenure of a Cardiff Royal Infirmary Research Fellowship in Medicine. It is a pleasure to acknowledge my indebtedness in particular to Dr. J. S. Lawrence. Dr. Joan M. Bremner, and the members of the Empire Rheumatism Council Field Research Unit; to the Board of Governors of the United Cardiff Hospitals for their generous help and ready provision of facilities; to the staff of the Medical Unit and Institute of Pathology of the Welsh National School of Medicine for secretarial and technical assistance; to Mr. P. D. Oldham, of the Medical Research Council, for statistical advice; to Dr. William Phillips for leave of absence; to all the people of Wensleydale who so willingly co-operated in this survey; and finally to Professor H. Scarborough, Professor A. L. Cochrane, and Dr. R. M. Hardisty for their constant encouragement, interest, and advice.

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CLINICAL TRIAL OF METHOSERPIDINE IN GENERAL PRACTICE

BY

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Methoserpidine ("decaserpyl"), a synthetic isomer of reserpine, is a hypotensive drug prepared by Velluz (Velluz *et al.*, 1958a; Velluz, Peterfalvi, and Jequier, 1958b; Velluz, 1959). Previous reports on the drug (Velluz *et al.*, 1958b; La Barre, 1960; Mir and Lewis, 1960) have shown that the hypotensive properties of the rauwolfia preparations have been retained while the undesirable side-effects have been practically eliminated.

Trials in 1959 and 1960 (Brun and Rondelet, 1959; Gros *et al.*, 1959; Mériel *et al.*, 1959; Merlen and Gérard, 1960; Tricot *et al.*, 1960) showed an effective reduction of diastolic pressure—that is, generally at least 20 mm. Hg in two-thirds of hypertensive patients. These reports mention marked subjective improvement—relief of headache, giddiness, and tinnitus, and a feeling of general well-being. Bradycardia in some cases was also noted. In these trials the dosage ranged from 15 to 60 mg. daily by mouth, 30 mg. daily being the most suitable dose in the majority of cases. Side-effects were uncommon. There were occasional instances of nausea and epigastric discomfort, and more rarely diarrhoea or nasal congestion. Previous reports refer to the absence of major depressant effects on the nervous system even with 100 mg. or more a day.

It has been our experience with hypotensive drugs in general practice that they do not on the whole achieve the results claimed for them on the basis of hospital trials. It would appear that the effect of a drug on a patient living a normal everyday life is very different from that on a patient undergoing hospital regimen. We found that small doses of many drugs in ambulant patients did not produce a significant or maintained hypotensive effect. Larger doses often produced unpleasant side-effects.

We decided to carry out a trial of methoserpidine on hypertensive patients drawn from three separate practices in Glasgow. The duration of the trial was one year. Many of the patients were known to be hypertensives. Practically all had subjective complaints due to hypertension. No patient was included in the trial who was already progressing favourably on alternative treatment.

Of the 48 patients treated, 43 suffered from benign essential hypertension. The other five were cases of hypertension with aortic incompetence, hypertension with thyrotoxicosis, pre-eclamptic toxaemia, pre-malignant hypertension, and malignant hypertension.

Method

The patients were initially assessed objectively and subjectively. They were seen weekly or fortnightly at first, and in some cases the intervals were later extended to a month. The initial dosage of methoserpidine depended upon the overall clinical assessment. The dose was increased or decreased at subsequent attendances until a suitable maintenance dose was achieved. From experience we found that 30 mg. in three divided doses was the best initial dosage in most cases.

To assess the hypotensive effect of the drug, the means of all the systolic and diastolic readings taken during the trial have been calculated for each patient and compared with the *lowest* level of blood-pressure previously recorded in the absence of any hypotensive drug therapy. This method of assessment has been used because, in the absence of a double-blind technique, it provided us with the best safeguard against introducing a bias into the results.

Results

The principal data in each of the 43 cases of essential hypertension are summarized in Table I. The frequency of the different dosage levels initially and that at the termination of treatment or of the trial are shown for comparison in Table II.

Hypotensive Effect.—The distribution of the degrees of mean reduction in the systolic and diastolic pressures is shown in Table III. There was a mean reduction in diastolic pressure of over 20 mm. Hg in 10 cases (the largest being 34 mm.) and of 10–20 mm. in 19 cases (including a patient who was also treated with guanethidine and hydroflumethiazide). The mean reduction in systolic pressure exceeded 20 mm. Hg in 24 patients, and in 10 of these it was greater than 40 mm.

TABLE I.—*Cases of Essential Hypertension*

Case No.	Sex and Age	Dosage (mg./Day)	Duration of Treatment (Months)	Minimal Untreated Blood-pressure (mm. Hg)	Mean Reduction in Blood-pressure (mm. Hg)	
					Systolic	Diastolic (% Reduction in Parentheses)
1	F 56	20–40	10	240/140	37	11 (8)
2	F 59	20–40	10	210/130	2	12 (9)
3	M 71	15–60	10	200/140	11	11 (8)
4	F 68	20–40	5	150/110	+4	7 (6)
5	F 67	20–40	10	210/130	12	10 (8)
6	F 60	20–40	9	190/130	9	18 (14)
7	M 59	10–30	8	180/110	41	26 (24)
8	F 54	20–40	10	180/115	14	11 (10)
9	F 63	30–60	7	280/160	52	18 (11)
10	M 62	20–40	8	170/110	12	10 (9)
11	M 56	20–40	5	180/110	31	13 (12)
12	M 55	30–40	4	170/110	11	2 (2)
13	M 57	20–40	5	160/110	10	8 (7)
14	F 48	15–40	4	160/110	+6	16 (15)
15	F 53	20–60	4	160/110	+1	5 (5)
16	F 63	15–40	10	180/110	+2	+3 (0)
17	F 62	15–30	9	150/120	+16	3 (2)
18	M 55	15–40	8	160/110	7	8 (7)
19	M 69	15	4	190/100	15	12 (10)
20	F 46	30–60	5	270/125	34	20 (16)
21	F 58	30–60	5	250/110	21	11 (10)
22	M 45	30	6	215/150	22	34 (23)
23	M 65	15	4	210/110	26	15 (14)
24	F 76	30	6	260/110	51	8 (7)
25	F 75	15–40	6	280/130	61	27 (21)
26	M 63	10–15	4	220/110	38	18 (16)
27	F 51	20–30	3	200/100	6	10 (10)
28	F 48	30–45	1	200/110	17	7 (6)
29	F 60	30–60	½	220/120	+11	2 (2)
30	F 60	15–30	10	260/120	68	20 (17)
31	F 65	15–20	4	260/130	53	30 (23)
32	F 53	10–20	4	225/120	54	26 (22)
33	F 71	10–20	6	250/120	65	20 (17)
34	F 69	10–15	3	230/100	33	8 (8)
35	F 59	20–30	1	205/115	40	32 (28)
36	F 71	15–30	2	230/120	51	20 (17)
37	F 67	10–30	10	205/118	21	21 (17)
38	F 66	15–30	11	220/115	43	28 (24)
39	F 44	15–30	6	240/130	37	22 (17)
40	F 61	30	5	180/110	15	5 (5)
41	F 69	15–30	5	240/130	21	8 (6)
42	F 40	30	3	230/120	22	9 (7)
43	F 45	20	1	175/110	37	25 (23)

TABLE II.—*Distribution of Dosages at Beginning and End of Trial Periods in 43 Cases*

	Dosage (mg./Daily)				
	10–15	20	30	40–45	60
At beginning	9	10	16	8	0
At termination	12	14	10	4	3

Cardiovascular Symptoms.—In five patients who were subject to attacks of angina pectoris the frequency of the attacks seemed to be reduced during methoserpidine therapy. The mean reduction in diastolic blood-pressure was 10 mm. Hg or more in three of these (Cases 5, 10, and 21) and less than 10 mm. in two (Cases 13 and 18).

Reduction in exertional dyspnoea appeared to result from the treatment in nine patients with this symptom (Cases 4, 5, 6, 17, 19, 21, 23, 24, and 25), and ankle oedema associated with effort dyspnoea, present in five (Cases 4, 17, 19, 37, and 39), disappeared or was much reduced. Of the 11 patients with improvement in one or both of these symptoms, the mean reduction in diastolic pressure was 10 mm. Hg or more in eight.

One patient (Case 17) who was subject to attacks of nocturnal dyspnoea, and who had atrial fibrillation for which she received digoxin, seemed to be less prone to the attacks after the addition of methoserpidine to her treatment.

Symptoms Associated with Hypertension.—Symptoms of a subjective nature associated with hypertension were experienced by 35 of the 43 patients. All but two (Cases 12 and 43) of these reported some relief during methoserpidine therapy. The frequencies of occurrence of the different symptoms and of their relief with treatment are shown in Table IV. Complete or almost complete remission of symptoms usually occurred, but sometimes either the improvement was partial or the relief obtained initially was not maintained.

TABLE III.—*Distribution of Reductions in Systolic and Diastolic Pressures in 43 Cases*

Mean Reduction in Pressure	Systolic	Diastolic
Over 20 mm. Hg	24	10
10–20 ,, ,,	9	19
Under 10 ,, ,,	10	14

TABLE IV.—*Symptoms Associated with Hypertension: Incidence and Relief with Treatment*

Description of Symptom	No. of Cases with Symptom	Improvement			Unimproved
		Definite or Complete	Partial or Unsustained	Total	
Headache	30	22	6	28	2
Dizziness	24	16	5	21	3
Physical fatigue	10	5	4	9	1
Difficulty in mental concentration	7	3	2	5	2
Palpitations	5	3	2	5	0
Acroparaesthesiae	2	2	0	2	0

Side-effects.—We did not observe any toxic effects from methoserpidine during the trial. One patient (Case 3) complained of dizziness only while receiving methoserpidine, but with this exception none of the patients developed any unpleasant symptoms during treatment. So far, this is the only hypotensive drug used by us in general practice that has produced such a lack of side-effects.

Other Cases of Hypertension

The main features of the cases in which the hypertension was due partly or wholly to conditions other than essential benign hypertension are shown in Table V.

In Case 44 methoserpidine produced a mild reduction in mean blood-pressure and relief from headaches. Attacks of paroxysmal nocturnal dyspnoea were not prevented. Case 45 showed a moderate reduction in mean blood-pressure, especially in the systolic level.

A useful reduction in blood-pressure was obtained in Case 46, and the pregnancy proceeded satisfactorily to

TABLE V.—*Data on Other Cases of Hypertension*

Case No.	Sex and Age	Diagnosis	Dosage (mg./Daily)	Duration of Treatment (Months)	Minimal Untreated Blood-pressure (mm. Hg)	Mean Reduction in Blood-pressure (mm. Hg)	
						Systolic	Diastolic
44	F 76	Hypertension with aortic incompetence	20–45	1	220/100	8	12
45	F 43	,, ,, thyrotoxicosis	20–30	2	230/130	37	17
46	F 31	Pre-eclamptic toxaemia	20–40	3	180/120	36	24
47	F 57	Premalignant hypertension	40	4	260/160	22	12
48	F 54	Malignant hypertension	20–40	2	260/140	0	0

term. Methoserpidine has been used by us in several cases of pre-eclampsia since the trial and has proved most satisfactory. In Case 47 methoserpidine alone produced a mild reduction in mean blood-pressure and relief from headaches, dizziness, and palpitations. Subsequently an adrenergic-blocking drug was added to the treatment to produce a greater reduction in blood-pressure. No beneficial effects were obtained with methoserpidine in Case 48. Side-effects from the drug did not occur in any of these patients.

Discussion

In a number of trials of methoserpidine, as of some other hypotensive agents, a reduction in the diastolic level of 20 mm. Hg has been regarded as the minimum required to signify a definite hypotensive effect. However, this degree of reduction of diastolic pressure has often been based on a comparison of a reading taken at the end of a course of treatment with a casual reading taken immediately before the course was begun. It seems to us that this allows chance fluctuations in blood-pressure to influence unduly the levels recorded both before and after treatment.

In our assessment of the effect of methoserpidine on the blood-pressure we have calculated the means of the systolic and diastolic readings taken each time a patient was seen while receiving the treatment. The average number of readings was eight, with a range of 2 to 16. This method minimizes the chances of distortion of the results caused by spontaneous fluctuations in blood-pressure. We feel, moreover, that this is a more appropriate method of assessment in general practice, where the doctor is concerned with the continuous care of the patient, and that to have relied on a final reading after completion of a course of treatment would have been particularly unsuitable in our trial. We have compared the means of the blood-pressure readings during treatment, not with the means of pre-treatment systolic and diastolic levels, but with the *lowest* pre-treatment levels previously recorded. It is unlikely that mean reductions below the latter levels could reflect to any extent spontaneous fluctuations in blood-pressure. Hence we regard a reduction in *mean* diastolic level of 10 mm. Hg or more as significant of a real hypotensive action of the drug.

On this basis we have found a hypotensive effect with methoserpidine in 29 (67%) out of 43 cases of essential hypertension. It is interesting to note that, despite the use of a variety of methods of assessment, the published reports on this drug contain a close similarity in the proportion of patients in whom a hypotensive effect is produced. As in our trial, the proportion has been found to be about two-thirds of cases by Merlen and Gérard (1960), Tricot *et al.* (1960), and Mignault (personal communication, 1960), and about three-quarters of the cases by Brun and Rondelet (1959) and Read (1961).

Of our 29 patients with essential hypertension in whom a hypotensive action of the drug was demonstrable, we would regard the reduction as definitely beneficial clinically in just over a half—that is, in at least one-third of all the patients with essential hypertension. We have judged this, firstly, by a reduction in the mean diastolic pressure to 100 mm. Hg which was obtained in 16 out of 40 patients (three patients were excluded as their minimal pretreatment diastolic level was itself 100 mm. Hg). A similar result is obtained by using the criterion suggested by Fife *et al.* (1960) that a reduction in blood-pressure levels of 16% or more could be regarded as "a clinically useful" hypotensive response. Such a response of 16% or more in the diastolic level was obtained in 15 of our patients. This is a better result than that obtained by Fife *et al.* with reserpine in a dosage of 1.5 mg. daily, in a trial also carried out in Glasgow, a reduction of 16% or more in diastolic pressure being obtained in only one-quarter of their cases (5 out of 20).

A remarkable property of methoserpidine that we have confirmed has been the subjective relief it affords to hypertensive patients. Nearly all our patients benefited from the treatment in this way. Exertional dyspnoea, sometimes associated with ankle oedema, headaches, dizziness, and palpitations, were the principal symptoms from which the patients obtained partial or complete relief. In addition, in five patients with angina pectoris the frequency of attacks seemed to decrease during the treatment. Our observations show that the relief from symptoms takes place quite independently of a reduction in blood-pressure. Similar observations have been made in all the previous clinical reports on methoserpidine, including an instance of relief from attacks of angina pectoris reported by Read (1961).

It is known that methoserpidine, like the natural rauwolfia alkaloids, has various effects on the circulation in addition to its hypotensive action. In particular, it slows the heart rate. It has also been beneficial in cases of Raynaud's syndrome (Peacock, 1960), and it is possible that, as with reserpine, symptomatic relief might be obtained in migraine and in some cases of thyrotoxicosis—conditions in which vascular changes also occur. We therefore suggest that the beneficial effect of methoserpidine on hypertensive symptoms may be attributable to its reversing circulatory changes with which these symptoms might conceivably be associated. This could certainly be the case, at least, when palpitations, and perhaps headaches and dizziness, associated with a tachycardia are relieved by the treatment.

An outstanding advantage of methoserpidine is its freedom from side-effects. All our patients felt generally well while receiving the drug, and the only side-effect observed was one instance of dizziness. Fife *et al.*, in their trial, recorded that the patients receiving reserpine complained more frequently of tiredness and of lethargy and drowsiness than the controls. The tendency for reserpine to cause lethargy and mental depression, as well as nasal congestion, loose stools, and other side-effects, is well known. With methoserpidine we did not observe any tranquillizing, depressant, or gastro-intestinal side-effects.

There was no evidence of patients acquiring tolerance to the drug. In fact, a reduction in the dosage required occurred more often than an increase. The most frequent dosage used at the beginning of treatment was 30 mg. daily, while the most frequent at the end of treatment was 20 mg. daily (Table II). However, there were individual variations in the optimal dosage level, 12 patients being satisfactorily controlled on as little as 10–15 mg. daily, whereas three required as much as 60 mg. daily.

Our experience with the drug in cases other than of essential benign hypertension is too limited to allow us to form any definite opinion. However, investigation of its possible value in pre-eclamptic toxaemia would seem to be worth while, and it may well have a place

as an adjuvant to ganglion and adrenergic blocking drugs in the treatment of premalignant and malignant hypertension.

Summary and Conclusions

A co-operative clinical trial in general practice carried out by three practitioners in Glasgow is reported.

The drug concerned was a new hypotensive agent, methoserpidine (" decaserpyl "), a synthetic isomer of reserpine.

The effect of the drug was investigated mainly in 43 patients with essential (benign) hypertension. A definite hypotensive action was demonstrated in approximately two-thirds of the patients and was judged sufficient to be certainly beneficial clinically in one-third.

Almost all the patients obtained symptomatic improvement. The drug was found to be virtually free from side-effects and tranquillizing action.

Dosage of the drug should usually be 30 mg. daily initially, it being subsequently increased or decreased, if required, within the range of 10–60 mg. daily.

The findings broadly confirm the results reported in other investigations of this drug. Our experience indicates that methoserpidine is a useful drug for the management of mild and moderate cases of essential hypertension in general practice.

We would like to express our appreciation to Roussel Laboratories Limited for making available supplies of decaserpyl, and to Dr. J. J. Segall and Mr. W. Kirk for their assistance.

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CLINICAL EVALUATION OF PROPATYLNITRATE IN ANGINA PECTORIS

BY

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Although many preparations have been investigated for use as long-acting coronary vasodilators in angina pectoris few have survived a controlled unbiased study. Many claims of success have been based on a subjective assessment by the patient of improvement in his anginal attacks. Apart from the frequent spontaneous fluctuations in this symptom in the natural course of ischaemic heart disease, there is ample evidence that improvement will occur in any patient with angina with any new preparation irrespective of its active or inert properties (Greiner *et al.*, 1950). The necessity for a controlled double-blind trial is therefore apparent. In addition, however, an objective assessment of the anti-anginal activity must be made which relies as little as possible on the patient's own interpretation of his progress, and this is best accomplished by some form of exercise-tolerance test.

With these considerations in mind it was decided to carry out a clinical evaluation of a new coronary vasodilator, propatylnitrate (" gina "), which is chemically related to both glyceryl trinitrate and erythrol tetranitrate. Preliminary experimental observations have indicated its effectiveness in producing coronary vasodilatation in animals, and clinically it has been found to give both rapid relief of pain in an acute attack of angina pectoris and a prophylactic sustained action (Nordqvist and Varnauskas, 1960). For the present study an exercise-tolerance test has been devised which is more physiological than the Master two-step test (Master and Oppenheimer, 1929).

Patients and Methods

Thirteen out-patients aged 43 to 70 with well-authenticated and typical features of angina pectoris were studied (Table I). The angina had been static for the previous 12 months. There were nine men and four women, and in all of them the presumptive cause was coronary artery disease ; one woman aged 43 (Case 12) had familial hypercholesterolaemia. Four patients had electrocardiographic evidence of previous myocardial infarction. All the patients were taking glyceryl trinitrate freely for their anginal attacks.

TABLE I.—*Age-and-Sex Distribution of Patients Studied*

Case No.	Age in Years	Sex	Duration of Angina
1	50	M	7 years
2	58	M	13 "
3	60	F	8 "
4	61	M	3 "
5	51	M	3 "
6	70	M	2 "
7	58	M	5 "
8	60	F	5 "
9	52	F	3 "
10	65	M	9 "
11	58	M	2 "
12	43	F	7 "
13	54	M	2 "

A double-blind technique was employed. Both the immediate and prolonged action of propatylnitrate were studied. In investigating the immediate action in relieving anginal attacks a comparison was made with glyceryl trinitrate tablets in treating attacks occurring both during normal activity and after exercise-tolerance tests. The sustained effect of the drug in reducing the frequency of anginal attacks was compared with that of pentaerythritol tetranitrate (PETN ; " mycardol ").

An initial control period of one month was allowed when no additional coronary vasodilators were taken apart from glyceryl trinitrate. In the next three months of the study, individual monthly supplies of tablets of identical appearance containing propatylnitrate, an inert placebo, and PETN were provided in random order, neither the patient nor the observer being aware of which drug was given. The dosage of propatylnitrate was 10 mg. sublingually four times daily. The patients

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were also supplied with a specific number of glyceryl trinitrate tablets. All patients attended monthly, and at each visit the number of glyceryl trinitrate tablets consumed in the previous month was checked by the observer, thus ensuring an objective assessment of the number of anginal attacks. In the subsequent two months of the study the patients were given, again in random order, a month's supply of either propatylnitrate or glyceryl trinitrate, both of identical appearance, and were asked to take one tablet sublingually whenever an anginal attack occurred. They were advised to take these tablets as freely as desired, and no other coronary vasodilator was allowed. A note was made of the monthly consumption as before, and, in addition, of the approximate speed of relief of angina as stated by the patient.

Exercise-tolerance tests were carried out at the beginning of the study and at monthly intervals. The test was a modification of the Master two-step technique, the patient stepping up and down two steps each 1 ft. (30 cm.) high. The patient was allowed to exercise at his own speed until he was stopped either by the onset of angina, occurring in most patients, or, in a few cases, by dyspnoea. The total number of circuits accomplished was recorded, as was the time taken. An electrocardiogram was obtained before starting the exercise, immediately afterwards, and at intervals of a minute until all electrocardiographic signs of ischaemia had disappeared. This time was noted. Leads II and V5 were used and recorded simultaneously. When angina occurred after the exercise a glyceryl trinitrate tablet was given and a note made of the time required for the pain to go. ST depression of the type and timing described by Wood (1956) was regarded as significant of ischaemia. The nature and the purpose of the tests were explained to all the patients.

The weight, resting pulse, and resting blood-pressure were also recorded in all patients at each monthly visit.

The final phase of the study was designed to assess the rapidity of relief of angina with propatylnitrate. A series of exercise-tolerance tests were carried out at fortnightly intervals in six patients who were on no additional coronary vasodilators apart from glyceryl trinitrate. Identical tablets of propatylnitrate, glyceryl trinitrate, and placebo were given in random order to relieve the angina induced by the exercise-tolerance test, and the time required for the pain to disappear was noted in each case.

Only one patient (Case 13) in the series was unable to undertake exercise-tolerance tests during the course of the study.

Results

Table II indicates the weekly consumption of glyceryl trinitrate tablets during the control period and while the patients were on propatylnitrate, PETN, and placebo. In six patients there was a fall in glyceryl trinitrate requirements with propatylnitrate, but this occurred also in seven patients on PETN and in seven on the placebo. The mean weekly consumption of glyceryl trinitrate did not differ significantly between each other. Table II also shows the weekly requirements of propatylnitrate and glyceryl trinitrate when these drugs were used alone, and although there was a reduction in frequency of angina with propatylnitrate this was not a significant fall, and was evident also with use of the disguised glyceryl trinitrate tablets.

TABLE II.—*Weekly Frequency of Angina in the Different Periods of the Study*

Case No.	Weekly Consumption of G.T. Tablets				Weekly Consumption of Other Tablets	
	Control Period	PPN q.d.s.	Placebo	PETN	PPN Alone*	Disguised G.T. Alone
1	22	22	15	14	6	15
2	7	10	7	—	8	8
3	15	14	10	7	11	6
4	61	42	38	37	10	33
5	23	10	10	19	25	28
6	10	10	11	7	10	8
7	16	13	5	15	16	15
8	25	48	48	32	25	25
9	14	21	16	15	19	28
10	14	15	18	21	27	23
11	27	19	18	42	18	17
12	62	63	58	61	68	56
13	10	7	10	3	10	10
Mean S.E.	23·5 ±4·4	22·6 ±4·8	20·3 ±4·7	22·8 ±4·7	19·5 ±4·5	20·9 ±3·8

PPN = Propatylnitrate. G.T. = Glyceryl trinitrate. * Only in anginal attacks.

The results of the exercise-tolerance tests are shown in Table III. The total amount of exercise increased, but not significantly with PETN, propatylnitrate used prophylactically, and the placebo. There was no significant difference apparent between the three preparations. When propatylnitrate was used alone there was a significant increase in the total amount of exercise ($P<0.05$), and this occurred with the disguised glyceryl trinitrate also ($P<0.05$), but there was no difference between the two drugs themselves. The mean rate of performance of exercise also increased significantly both with propatylnitrate used alone and with the disguised glyceryl trinitrate ($P<0.05$).

When propatylnitrate was given prophylactically with standard glyceryl trinitrate for the acute attacks of angina, the difference in rate of performance was no longer significant. Nor was there a significant change with PETN.

TABLE III.—*Results of Exercise-tolerance Tests*

Case No.	Total No. Circuits						Mean Time/Circuit (Seconds)					
	Control	PPN q.d.s.	Placebo	PETN	PPN* Alone	Disguised G.T. Alone	Control	PPN q.d.s.	Placebo	PETN	PPN* Alone	Disguised G.T. Alone
1	9	15	17	—	38	—	5·6	4·5	5·6	—	3·2	—
2	—	41	50	—	40	48	—	2·5	2·5	—	2·3	2·3
3	31	38	63	69	80	—	2·7	2·4	2·4	2·6	2·4	—
4	27	26	25	—	20	28	3·3	5·2	5·4	—	3·0	2·6
5	16	37	32	22	23	29	4·0	2·2	2·3	2·8	2·8	2·7
6	35	40	38	40	41	50	3·0	2·0	4·0	2·3	2·2	2·1
7	25	23	15	18	23	23	4·0	5·0	3·0	6·8	4·4	4·1
8	21	35	—	46	45	44	2·1	2·0	—	2·1	2·2	3·6
9	21	35	25	30	35	40	2·6	2·4	3·0	2·5	2·6	2·2
10	40	40	35	13	43	40	2·9	1·9	1·7	2·3	1·8	1·5
11	21	21	—	21	20	17	3·8	3·7	—	6·0	3·5	3·2
12	17	15	10	40	15	30	3·0	3·0	3·5	2·5	2·7	2·8
Mean ± S.E.	24·2 ± 2·4	30·5 ± 2·9	31·0 ± 5·1	33·2 ± 5·9	35·2 ± 5·1	34·9 ± 3·5	3·4 ± 0·2	3·1 ± 0·3	3·3 ± 0·4	3·3 ± 1·0	2·8 ± 0·1	2·7 ± 0·2

* Only in anginal attacks.

Table IV shows that ischaemic changes followed exercise in all 12 patients in the control period. In five the ischaemic changes became more pronounced after a prophylactic course of propatylnitrate; only one patient (Case 9) showed an improvement with propatylnitrate, and in her case improvement occurred with PETN also.

TABLE IV.—*Severity of Ischaemic Changes on the Electrocardiogram During Exercise Tolerance Tests*

Case No.	Control Period	PPN q.d.s.	Placebo	PETN	PPN* Alone	Disguised G.T. Alone
1	+	++	+	N.D.	+	N.D.
2	+	+	+	N.D.	+	+
3	+	+	+	+	+	N.D.
4	++	++	+	N.D.	++	++
5	+	++	++	+	++	++
6	+	+	+	+	+	+
7	+	+	+	+	+	+
8	+	++	N.D.	+	++	++
9	++	+	+	+	+	++
10	+	++	+	+	++	++
11	+	++	N.D.	++	++	++
12	+	+	+	+	+	+

N.D. = Test not done. * Only in anginal attacks.

The mean time taken for the electrocardiographic changes of ischaemia to revert to normal was shortest when propatylnitrate was used alone and also after a course of PETN, but the time did not differ significantly from the control period (Table V). Similar findings were evident when the time taken for relief of anginal pain was considered, but again this was not a statistically significant finding.

In the final study of rapidity of relief of angina induced by exercise-tolerance tests, propatylnitrate produced a more rapid effect than glyceryl trinitrate, although the difference in the mean time taken for relief was just not significant (Table VI). Comparison of propatylnitrate and placebo, however, showed a significantly faster relief of angina with the former ($P<0.05$); although glyceryl trinitrate produced more rapid relief than the placebo the difference was small and not a significant one.

There were no changes in weight, pulse, or blood-pressure attributable to propatylnitrate in any patient during the course of the study, and no consistent toxic effects or side-effects were encountered. In fact, several patients experiencing unpleasant side-effects with glyceryl trinitrate had no similar reactions when propatylnitrate was used to abort any anginal attack.

Discussion

It has been stated that in the administration of any anti-anginal agent the therapeutic effect is directly related to the personality of the physician and his own belief in the curative powers of the drug together with the suggestibility of the patient and the intensity of the patient's desire to be cured (Greiner *et al.*, 1950). This view is supported by Cole, Kaye, and Griffiths (1958), who studied the effects of four coronary vasodilators in patients with angina pectoris, and found a decrease in the frequency of chest pain regardless of whether an active drug or placebo was being administered. The importance of a double-blind technique is therefore plain. More important still is an objective index of improvement provided by an exercise-tolerance test.

TABLE VI.—*Speed of Relief of Angina Induced by Exercise-tolerance Tests with PPN, Placebo, and Disguised Glyceryl Trinitrate Tablets*

Case No.	PPN (Seconds)	Placebo (Seconds)	Disguised G.T. (Seconds)
1	55 90 120	135	85 105
3	10	50	160
5	50 60 35 45	100	72 60
	75 125 150	195 155	57
11	60	110	130 135
12	30	155 120 40	218
Mean ± S.E.	71·8 ± 10·8	117·8 ± 16·5	113·6 ± 20·6

The Master two-step test has been criticized as being unphysiological and also for not taking into account differences in habits of exertion, in physical capacity, and in training of patients; in addition, the amount of exercise carried out by the patient within the prescribed time may be insufficient to produce electrocardiographic changes of ischaemia. Fife, Howitt, and Stevenson (1958) claim that this test often produces inconclusive results. The exercise-tolerance test employed in the present study has the advantage of a more physiological performance of exertion at the patient's own rate and within the limits of his own capacity. Results are more conclusive as electrocardiographic evidence of ischaemia developed in all 12 patients exercised during the control period. The patient stops at the onset of angina, and although it is claimed that exercise-tolerance tests are not without risk in patients with angina (Grossman and Grossman, 1955) this risk is very slight. Objections have been raised against exercise-tolerance tests in anginal patients, owing to this slight potential hazard, but one is, after all, only carrying out, under close medical supervision,

TABLE V.—*Duration of Electrocardiographic Changes and Angina after Exercise-tolerance Tests*

Case No.	Time for E.C.G. Changes to Revert to Normal (Minutes)						Time for Disappearance of Angina (Minutes)					
	Control	PPN q.d.s.	Placebo	PETN	PPN* Alone	Disguised G.T. Alone	Control	PPN q.d.s.	Placebo	PETN	PPN* Alone	Disguised G.T. Alone
1	9·0	8·0	8·0	—	5·0	—	4·0	2·3	1·7	—	2·0	—
2	—	7·0	1·00	—	6·0	8·0	—	4·0	4·0	—	2·5	2·5
3	9·0	9·0	—	4·0	5·0	—	0·8	1·8	D	1·8	0·1	—
4	6·0	7·0	6·0	—	6·0	5·0	5·0	5·8	5·0	—	5·0	5·0
5	4·0	5·0	6·0	4·0	4·0	4·0	0·8	1·0	0·5	0·8	1·0	0·5
6	3·0	4·0	4·0	4·0	4·0	4·0	2·0	2·0	2·5	2·5	2·1	2·0
7	4·0	2·0	4·0	1·0	1·0	1·0	2·0	2·0	2·0	1·0	1·0	1·0
8	4·0	6·0	—	7·0	4·0	6·0	5·0	D	—	D	D	D
9	7·0	6·0	6·0	5·0	—	7·0	0·7	D	D	D	D	D
10	5·0	4·0	4·0	4·0	4·0	5·0	D	D	1·3	1·8	D	D
11	3·0	5·0	—	5·0	4·0	5·0	D	2·3	—	2·0	1·8	5·0
12	2·0	2·0	1·0	1·0	1·0	3·0	D	1·5	2·5	3·3	1·7	3·0
Mean ± S.E.	5·1 ± 0·7	5·4 ± 0·6	5·4 ± 0·9	3·9 ± 0·4	4·0 ± 0·6	4·8 ± 0·6	2·5 ± 0·9	2·5 ± 0·5	2·4 ± 0·5	1·9 ± 0·3	1·9 ± 0·5	2·7 ± 0·7

* Only in anginal attacks. D = Dyspnoea.

exercise which the patient is in the habit of undertaking daily without any supervision whatsoever.

In over 200 personally supervised tests of the type described in this study, no ill effects were noted.

In the present study there was a fall in the mean weekly glyceryl trinitrate requirements with propatylnitrate, PETN, and placebo, in accordance with the findings of Cole *et al.* (1958). The differences in the frequency of angina, however, between propatylnitrate or PETN on the one hand and the placebo on the other were not significant. Similarly there was no significant increase in the total amount of exercise performed in the exercise-tolerance test with either propatylnitrate or PETN. When propatylnitrate was used alone the rate of performance of exercise did increase significantly, but this apparent improvement was not reflected in the electrocardiogram. In fact, in four of the eight patients showing an increase in rate of performance with propatylnitrate the ischaemic changes became more marked, suggesting that the acceleration of exertion occurred without a corresponding improvement in myocardial blood supply.

A course of propatylnitrate reduced the duration of subjective and objective evidence of myocardial ischaemia induced by exercise. In addition propatylnitrate gave more rapid relief than glyceryl trinitrate when used in treating an acute anginal attack produced by an exercise-tolerance test. These results conflicted with the subjective assessment of the patients, most of whom claimed that propatylnitrate was slower in relieving an anginal attack than glyceryl trinitrate. This illustrates the difficulty in assessing the value of drugs used in relieving angina and the unreliability of the patient's own evaluation or interpretation of his progress.

Nordqvist and Varnauskas (1960) found propatylnitrate to be of value both in relieving acute attacks of angina and in prophylaxis in angina pectoris. The present study does not wholly support these findings, as there was no conclusive evidence of its efficacy as a long-acting coronary vasodilator. The investigation does, however, indicate the possible value of propatylnitrate in the acute attack of angina pectoris. It may be of particular value in those patients experiencing unpleasant side-effects with glyceryl trinitrate, and also in those chronic severe anginal patients no longer experiencing relief with glyceryl trinitrate.

The failure of PETN either to alter significantly the frequency of anginal attacks or to improve performance in exercise-tolerance tests is of interest, and supports similar results reported by Dewar, Horler, and Newell (1959).

Summary

The clinical effect of propatylnitrate, a new coronary vasodilator, has been studied in 13 patients with angina pectoris. A double-blind technique was employed, and the use of the drug was investigated both for immediate relief of acute angina and for its more sustained action. To ensure an objective assessment an exercise-tolerance test has been devised which allows the patient to exercise at his own speed and within the limits of his own capacity.

There was no significant change in either the frequency of anginal attacks or the total amount of exercise undertaken while the drug was in use.

When propatylnitrate was taken freely, however, there was a significant increase in the rate of performance of exercise but no corresponding improvement in the electrocardiographic changes of ischaemia. Pentaerythritol tetranitrate (PETN), which was included in the double-blind study, also failed to influence significantly either the frequency of anginal attacks or the exercise-tolerance tests.

Propatylnitrate was more rapid than glyceryl trinitrate in relieving acute attacks of angina induced by exercise-tolerance tests.

It is concluded that propatylnitrate may be of value in treating acute attacks of angina. Its use is suggested in patients experiencing unpleasant side-effects with glyceryl trinitrate and in those who have become resistant to that drug. No evidence has been found to support its use as a long-acting coronary vasodilator.

The importance of a controlled double-blind study and objective criteria of improvement in the assessment of an anti-anginal drug is pointed out.

I am indebted to Dr. D. Verel for his encouragement and helpful advice; to the electrocardiographic technicians of the Sheffield Region Cardiovascular Centre for their willing co-operation in this study; and to Dr. K. Boheimer, of Bayer Products, for the supply of "gina" tablets.

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"Should infectious disease continue to be taught? Surely it might be argued that this is one aspect of medicine of which it can truly be said that improvements in sanitation and hygienic living, the application of the preventive effects of immunizing procedures and the discovery of specific forms of chemotherapy—such advances have eradicated from the community the major part of man's communal diseases and causes of death. And yet, even as one makes that boast one is reminded that there are large areas of the world where infectious diseases of one kind or another still constitute the main menace; and we must remember that the graduate may practise in any part of the world. But, even in our own country, it is still the laymen's jibe that the commonest infection of all, the "common cold," still marches through the community undeterred by the advances of modern medicine, and this should remind us all that virus infections remain very largely uncontrolled. There is indeed a necessity for the student to be made aware of the fact that when, as a doctor, his telephone rings, on a quarter to one-third of the occasions it will be a bacterium or virus which has occasioned its ringing." (*Annual Report on the Work of the Infectious Diseases Hospitals, 1960*, submitted to the Western Regional Hospital Board by Professor T. Anderson.)

FAILURE OF PROPATYLNITRATE AND PENTAERYTHRITOL TETRANITRATE TO PREVENT ATTACKS OF ANGINA PECTORIS

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There is at present no widely accepted medicament which can be relied upon to abolish or diminish the frequency of attacks of angina pectoris. We report here the result of a double-blind controlled clinical trial of a new drug, propatylnitrate. It was originally called "etrynit," but prior to marketing in this country the name was changed to "gina." We have previously shown (Sowton and Oram, 1961) that it is as effective as glyceryl trinitrate in the treatment of an acute attack of angina pectoris, and that on rare occasions it has certain advantages over that drug.

Nordqvist and Varnauskas (1960) carried out clinical investigations of propatylnitrate on 65 patients for two years in Scandinavia and concluded that it is as useful as glyceryl trinitrate in the acute angina attack and that the frequency of attacks is much reduced for five hours after a 10-mg. tablet. They consider 10 mg. of propatylnitrate to be more effective than 30 mg. of erythritol tetranitrate, which in turn they found to be more effective than 30 mg. of pentaerythritol tetranitrate (PETN; "mycardol").

Method

The trial was designed to compare 10 mg. of propatylnitrate against a placebo and also against 30 mg. of PETN.

Thirty patients (22 men and 8 women) took part in the trial, all attending a cardiac clinic because of angina pectoris. The age limits were 40 to 71 (men) and 46 to 66 (women). The diagnosis of angina was made on a typical history accompanied by electrocardiographic evidence of ischaemic heart disease in all cases. No patients with aortic valve disease or anaemia (below 80% haemoglobin) were included, and in each patient the frequency of attacks of angina had remained fairly stable for at least two months. All patients were familiar with the use of glyceryl trinitrate for the treatment of acute attacks.

The three drugs were prepared by the manufacturer as apparently identical tablets, and supplied under the labels A, B, or C. They were dispensed in boxes identified only by a number, the boxes being filled and distributed in random order by the use of Fisher and Yates's (1957) statistical tables, in such a way that each patient received three boxes, each containing one drug.

Patients were asked to take one tablet sublingually three times a day whether they had pain or not, and to use glyceryl trinitrate for acute attacks. Each box contained enough tablets for one week, and the boxes were used consecutively, starting with the lowest-numbered box. Patients kept notes during the trial and returned to the clinic after three weeks, when they were asked which tablets had been most effective and which least effective in preventing attacks of pain; they were also asked if any side-effects had been noticed.

We decided to use this method of assessment, as it is the pain of which patients with angina pectoris complain that we hope to treat. So-called objective tests, depending, for example, upon the development of electrocardiographic changes or on alterations in effort tolerance, are not necessarily closely related to the production of pain (Master and Rosenfeld, 1961). Often, too, such tests depend on the decision of the patient when to stop exerting himself. It is apparent that there can be no accurate objective test of a symptom.

Results

We assessed our results by the method of sequential analysis (Armitage, 1954; Snell and Armitage, 1957). The drugs were compared in pairs and the results plotted on a sequential analysis chart with boundaries corresponding to a 5% significance level. Until the trial had finished the drugs were known only as A, B, or C, but the identities were then determined from a key supplied by the manufacturers. Analysis in this manner failed to show a significant difference between the three preparations:

Propatylnitrate and Placebo		PETN and Placebo		Propatylnitrate and PETN	
Propatylnitrate better	8	PETN better	11	Propatylnitrate better	8
Placebo better	17	Placebo better	13	PETN better	15
No difference	5	No difference	6	No difference	7

Discussion

Opinions regarding the value of PETN as a preventive of angina pectoris vary from it being of considerable value (Wingfield and Goldfoot, 1957; Johnson and Sevelius, 1960) to being useless (Dewar *et al.*, 1959; Phear and Walker, 1960). Winsor and Scott (1955) found PETN to be of definite value when administered sublingually, and this route was used by us to enable a double-blind technique to be employed. During the course of the trial some patients became so impressed with one set of tablets that they pleaded by letter and telephone for further supplies. One patient claimed that his average consumption of glyceryl trinitrate fell from 12 to 2 tablets a day when taking propatylnitrate but rose again to 12 a day when his supply ran out. This effect was obtained on three occasions and did not occur when he was supplied with PETN or with placebo tablets.

Side-effects were fairly evenly limited to all three preparations and usually consisted of headache or giddiness. Eight of the 30 patients found one tablet to be very good indeed at preventing attacks, this action being attributed to propatylnitrate in two cases, to PETN in three, and to the placebo in three. Although our results differ from those of the Scandinavian workers in regard to the prophylactic use of propatylnitrate, they are in complete agreement with the conclusions reached by Sandler (1961), who has also fully investigated propatylnitrate, PETN, glyceryl trinitrate, and a placebo at Sheffield by a double-blind technique.

It appears that propatylnitrate is a potent drug for the relief of acute attacks of angina pectoris but is of little or no value in prophylaxis. In our opinion there is as yet no drug which can be relied upon to abolish or diminish the frequency of attacks of angina pectoris.

Conclusion

In the doses used sublingually propatylnitrate and PETN did not differ significantly from a placebo in abolishing or diminishing the frequency of attacks of angina pectoris.

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FATTY CHANGE IN THE MYOCARDIUM OF THE NEWBORN

BY

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Recent perinatal mortality surveys have shown that in many babies dying either during or soon after delivery no cause for death apart from asphyxia can be found. Our own figures for the Glasgow Royal Maternity Hospital reveal that at least 33% of perinatal deaths have to be classified as such. Yet the term is a loose one, and the findings at necropsy vary greatly. In many, however, appearances suggestive of cardiac failure are seen. In these cases there is distension of the right heart, especially the atrium, together with congestion of the great veins. Enlargement of the liver is not generally noted, but on section blood pours from the cut surface. One other feature suggesting venous congestion is the marked distension of the umbilical vein in the ligamentum teres. This appearance was seen in babies dying shortly after delivery and was even more marked in other cases showing hyaline membrane formation. This conception of cardiac failure as a factor in death of the newborn has been suggested by many clinical observers (Rowe and James, 1957; Burnard, 1959; Brown, 1959), and Lendrum (1955) was of the opinion that it was primarily due to a left heart failure.

Obviously this failure is functional in nature, but it is the purpose of the pathologist to find, if possible, some morphological counterpart for the clinical and post-mortem appearances. It was therefore decided to examine the myocardium in these cases to determine whether the failure was accompanied by histological change or not.

Material and Methods

Altogether 72 cases were studied, 15 being stillbirths and 57 neonatal deaths. These were unselected and included infants of all degrees of maturity. Macerated stillbirths were excluded from the survey. It is the custom in this hospital to place the bodies of all babies in a refrigerator within one hour of death. Necropsies were carried out within 24 hours. Longitudinal blocks through atrium and ventricle were taken from both sides of the heart, the left block longer than the right in order to identify the side of origin. Material was fixed in buffered formalin (*p*H 7) and also in picric alcohol. Frozen sections were stained for fat with Sudan IV and paraffin blocks with haematoxylin and eosin and lead tetra-acetate Schiff (L.T.A.S.). Material fixed in picric alcohol was examined for glycogen, using Best's carmine stain. Later in the survey, however, this was discontinued, as it was found that L.T.A.S. gave a relatively good estimate of the amount of glycogen present. The grading of both fat and glycogen was made on a 0, +, ++, +++ basis and was carried out in advance of the routine post-mortem histology without reference to the individual records (Fig. 1). In this there was less chance of the grading being influenced.

Results

On analysing the findings it soon became apparent that the amount of glycogen present varied greatly from case to case, but fatty change followed a much more definite pattern. In no instance did the left heart ever show more fat than the right, nor the atrium more than the ventricle. Indeed, in 50% of the cases the right ventricle showed most change, while in the remainder both ventricles were equal. Apart from the fact that the average duration of life was shorter—namely, 28 hours

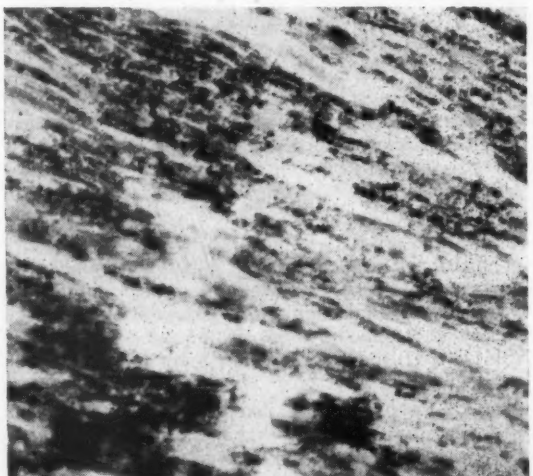

FIG. 1.—Fatty change in the myocardium, grade +++. (Frozen section stained with Sudan black.)

—when fatty change predominated in the right heart and increased to 40 hours when both ventricles were equal, no difference could be seen in these two groups. Thus it seems that fatty change appears earlier in the right heart.

As already mentioned, there were 57 unselected neonatal deaths in the series; the results of their analysis are shown in Table I. Also included are six stillbirths, which are discussed later. All cases were graded according to the amount of fat present in the right ventricle.

TABLE I.—*Cause of Death and Incidence of Fatty Change in the Right Ventricle in 57 Neonatal Deaths and 6 Stillbirths*

Cause of Death	No. of Cases	No. of Cases Positive	No. of Cases Strongly Positive
Hyaline membrane disease	21	17	11
Asphyxia	7	5	3
Haemorrhages	15	7	2
Rhesus incompatibility (4 stillbirths)	8	6	3
Unavoidable foetal blood loss *in utero* (1 stillbirth)	3	3	2
Placental insufficiency	2	2	1
Congenital heart disease	3	3	3
Pulmonary hypoplasia (1 stillbirth)	4	2	0

Hyaline Membrane Cases

The largest group consisted of 21 cases with hyaline membrane disease. All were premature and showed post-mortem changes of cardiac failure, with the exception of two, where it was presumed that large terminal intraventricular haemorrhages had relieved the venous pressure. Apart from four cases, which are discussed later, fatty change was present in all the hearts. Thus 17 (81%) were positive—11 of them (52%) strongly positive.

When the cases were divided into three groups according to the amount of fat present in the right ventricle, each presented a distinct clinical picture (Table II). The first group of five cases with marked fatty change were typical examples of the so-called "hyaline membrane syndrome." Initially all the babies were in good condition, but after a few hours they developed respiratory distress and deteriorated, dying approximately 43 hours after delivery. Hyaline membrane formation was marked in each of these babies.

In the second group of six cases showing moderate amounts of fat the condition of the child at birth was variable. Occasionally slight improvement occurred, but deterioration eventually set in and the babies died some 30 hours after delivery, the hyaline membrane being if anything less prominent, but variations were wide.

In the third group of six cases with only slight fatty change the condition of the babies was never good and all died within a few hours of delivery. The hyaline membrane was patchy and areas of primary atelectasis were frequent. One felt that the latter was more important than the membrane itself in causing the baby's death.

TABLE II.—21 *Cases of Hyaline Membrane Disease*

Amount of Fat	No. of Cases	Average Maturity (weeks)	Average Weight of Baby (g.)	Average Condition of Baby	Average Amount of H.M.	Average Duration of Life (hours)
+++	5	31·5	1,558	Good—slow deterioration	+++	43
++	6	31	1,363	Variable—slow deterioration	++	30
+	6	30·5	1,567	Poor	+-++	9
0	4	?	2,040	Oedema ++. Serum proteins 4·9 g.%	++	29
		30	1,420	Poor. ?Foetal blood loss	+	5
		31	1,240	Poor. Alveolitis placentitis	++	9½
		32	1,050	Poor. Neuroblastoma—one adrenal	+	3

It was remarkable how easily each of the above groups could be identified and how they showed this direct relationship between the degree of fatty change, the duration of life, and to a less extent the amount of membrane formation.

Asphyxial Deaths

There were seven neonatal deaths in which the post-mortem findings showed appearances suggestive of asphyxia. Five of the babies were premature. All had signs of cardiac failure, and fatty change was present in the myocardium in five (71%); it was marked in three (43%). In the remaining two cases, which were negative, intrapulmonary haemorrhage had occurred. The number in this group is too small for further analysis, but I had the impression that the fatty change could once again be related to the duration of anoxia.

Haemorrhage

The 15 cases in this group presented a very varied picture at necropsy. In four babies with cerebral birth injury cardiac failure was not a feature, and even in the remainder, where the haemorrhages were asphyxial in origin, as in intraventricular haemorrhage, signs of venous congestion and cardiac failure were not usually found. Neither was fatty change in the myocardium prominent. In only two cases was it marked, and in both these babies the haemorrhages were slowly cumulative and asphyxial in origin.

Rhesus Incompatibility

Eight cases were included in this group, four stillbirths and four neonatal deaths. Unlike the majority of stillbirths examined, the stillborn hydropic babies in this group showed evidence of fatty change in the myocardium. In all four the myocardium was pale and there was evidence of hypertrophy. In two of the neonatal deaths the infants showed hyaline membrane formation and they also had marked fatty change in the heart. The remaining two were negative for fat, and, though no valid explanation can be given, it is interesting to note that both babies were delivered by caesarean section. They lived for seven and nine hours respectively.

Gross Oxygen Lack in Utero

Two conditions likely to cause gross foetal anoxia are considered here. In the first group, three babies died of anaemic anoxia due to unavoidable foetal blood loss. All were extremely pale and the great vessels and heart were empty at necropsy. Fatty change was seen in the myocardium and in two of the three cases it was marked. One of these was a stillbirth. The others survived only a few hours.

In the other group of two cases the anoxia was thought to be due to placental insufficiency. This condition is always difficult to assess, but in addition to the placental changes, which were obvious, the babies were long, thin, and wizened. They lived only 12 and 45 hours respectively. Though both showed evidence of fatty change in the myocardium, more was found in the baby which died the sooner.

Congenital Heart Disease

All three babies with congenital heart disease showed marked fatty change in the myocardium. Deaths in this group occurred between the first and third days, and only one baby was premature.

Pulmonary Hypoplasia

Two cases of anencephaly and two with renal abnormalities are included in this group. All showed pulmonary hypoplasia (Potter, 1952). The renal abnormalities were bilateral polycystic kidneys and renal agenesis, and there was also some evidence of cardiac hypertrophy.

One of the anencephalics lived one and a half hours. Despite this short interval, some fatty change was present in the right heart, while none was seen in the left. The other anencephalic was stillborn and showed no evidence of fatty change.

Both babies with renal abnormalities were liveborn. The infant with renal agenesis lived half an hour and showed slight fatty change in the right heart, but not in the left. No fatty change occurred in the case of polycystic disease of the kidney, and this baby lived for one hour. However, here the pulmonary hypoplasia was less marked, the lungs weighing twice as much again as those in the cases of renal agenesis.

Stillborn Babies

Nine fresh stillbirths, two of them premature, were also examined, and the hearts of all these babies showed no evidence of fatty change.

Glycogen

So far the amount of glycogen found has not been considered. This varied greatly throughout the heart. Highest concentrations were noted in the papillary muscles and in the atria. Slightly less was found in that part of the ventricle immediately beneath the endocardium, and this decreased towards the pericardial surface. The actual amounts varied widely in left and right heart, and no one side was consistently the higher. This made assessment difficult.

Some of the variability in results may in part be due to post-mortem glycolysis, although, in view of the refrigeration, this ought to have been minimal. However, taking this into consideration it is interesting to note that those cases showing the most marked fatty change apparently also had an extreme degree of glycogen depletion. This is shown graphically in Fig. 2. Here it can be seen that as the fatty change increased so the incidence of complete glycogen depletion rose in each group and when fatty change was marked 73% of cases showed no stainable glycogen.

Discussion

One of the features of this analysis of fatty change in the heart of newborn babies is the similarity shown by the deaths due to asphyxia and hyaline membrane. Evidence of cardiac failure is seen in both and is associated with an atelectasis which may be primary or secondary, depending on the type of case. In each, fatty change in the heart is marked and increases with the duration of life. Glycogen depletion is also a prominent finding in both. Broadly speaking, though the initial processes may be different in these two conditions, it is possible that, terminally at least, the same factors may be present. Bound *et al.* (1956) compared the effects of oedema and haemorrhage seen in asphyxial lungs with those of hyaline membrane formation and found they were all remarkably similar. These authors actually stated that the one term "pulmonary syndrome" should cover all three conditions. Indeed, there is no clear line of demarcation between each group, and this is evident in the present survey.

In the six hyaline membrane cases with +fat it is doubtful if the very patchy membrane formation is of any significance at all. These babies are really dying of a primary atelectasis and ought to be included in the asphyxial deaths. Ranström (1953) was probably the first to draw attention to this group. He described in detail the histological appearance of the lungs, but did not analyse his findings further, though he felt the membrane was less important as a cause of death. Thus combinations of the two conditions occur, and, even in asphyxial deaths, hyaline masses, which have similar staining properties to that of the membrane, may be seen lying in partially collapsed alveoli.

Since there is this close association and lack of clear demarcation between the asphyxial and hyaline membrane deaths, I wonder if some common factor may not be present in each. The post-mortem appearances in both groups indicate a right heart failure, and underlying this there is the occurrence of atelectasis, sometimes primary, sometimes secondary, frequently mixed. This atelectasis is likely to have a double effect. There will be varying degrees of anoxia with consequent effects on metabolism, and intrapulmonary pressure will almost certainly be high (Rowe and James, 1957; Adams and Lind, 1957). In pulmonary hypoplasia similar conditions probably also exist, but here the inability of the lungs to expand, and not atelectasis, is responsible for the raised intrapulmonary pressure and possible increased load on the right heart.

This being so, it is interesting to note that fatty change was also found in all three cases of congenital heart disease. From the above it seems reasonable to suggest that an excessive load was placed on these hearts, thus increasing their metabolic demands, but owing to their inadequately maintained circulation and consequent anoxia their metabolism was probably deranged.

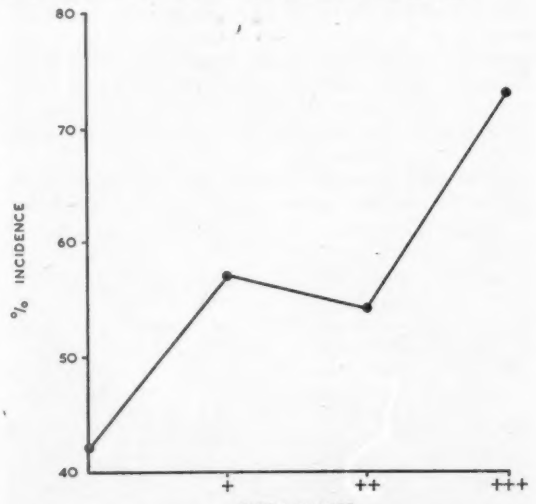

FIG. 2.—Incidence of glycogen depletion in relation to fatty change.

On the other hand, in the cases of rhesus incompatibility, placental insufficiency, and foetal blood loss *in utero* a high degree of anoxia must have existed even before birth, and it is possible that here the heart is already damaged and unable to maintain ordinary pressures. In the cases of rhesus incompatibility the infants were also extremely oedematous, and the obviously increased blood volume would add to the cardiac difficulties.

In contrast to cases of foetal blood loss *in utero* are those babies who die of haemorrhage in the neonatal period. Here the picture is not generally one of persistent or progressive anoxia, nor is there usually any evidence of cardiac failure at necropsy. It is not surprising that fatty change in the myocardium was infrequent and of mild degree.

It is more difficult to explain why certain cases of hyaline membrane disease do not conform to the general pattern. It will be remembered that there were four such cases in which no evidence of cardiac failure or of fatty change in the myocardium was seen. No real explanation for these cases can be offered, but it may be that the mechanism of formation of the membrane differed in these babies. Papers by Gitlin and Craig (1956), Van Breemen *et al.* (1957), and Carone and Spector (1960) have suggested that the membrane has an endogenous vascular origin, and this idea is now generally accepted. This being so, it is quite conceivable that general factors giving rise to pulmonary oedema, as well as local conditions peculiar to the pulmonary circulation, may play a part in membrane formation. Table II shows that in all four babies complicating factors were present and that each of these might well have influenced the development of pulmonary oedema. In these circumstances there might well be little obstruction to the pulmonary circulation and no increase in cardiac work.

Before concluding, it should be pointed out that it has not been the purpose of this paper to consider fat metabolism or fatty change in the neonate in any great detail. On the other hand, it does seem that in many cases some derangement of cardiac metabolism occurs before death in the newborn and that this can at least in part be related to anoxia and increased cardiac effort. It is independent of the maturity or nutritional state of the child and is not present in stillbirths, apart from a few expected exceptions. Experimental work on cardiac metabolism indicates that the heart does not use glucose directly—at least not to any great extent (McGinty and Miller, 1932). Under normal conditions lactic acid is the final product which is utilized, but it seems likely that another source of energy is fat (Cruickshank, 1936).

Whatever the intimate details of the metabolic process, it seems obvious that, in the circumstances prevailing, fat is transported to the myocardium under the stimulus of energy demands. Possibly, owing to anoxia, catabolism does not keep pace with the supply, thus leading to the deposition of fat in a stainable form. This is in line with modern thought on so-called "fatty degeneration" of the myocardium (Dible and Gerrard, 1938). Only in conditions of great stress is glycogen called upon as an emergency fuel (Fletcher and Waters, 1938). If this is so, it may explain why extreme glycogen depletion was a late feature in some of our cases where fatty change was marked. Of course it is realized that the histological assessment of glycogen is fraught with difficulty, and no definite claims can really be made in this respect at present, but it is interesting to note that the distribution pattern throughout the heart corresponds to that of chemical analysis (Cruickshank and Shrivastava, 1930; Blume, 1934).

Summary

Fatty change in the myocardium is a fairly constant feature in neonates showing evidence of cardiac failure at necropsy.

It was seen in babies dying of asphyxia, hyaline membrane disease, haemolytic disease of the newborn, unavoidable foetal blood loss *in utero*, placental insufficiency, congenital heart disease, and pulmonary hypoplasia.

It was not a prominent feature in deaths due to haemorrhage in the neonatal period, and with few exceptions was not found in stillbirths.

When present, fatty change tended to occur earlier and was more pronounced in the right heart. It is suggested that this may be related to raised pressure on the right side and increased cardiac effort resulting from atelectasis, together with the effects of anoxia itself. The extent to which each factor contributes will vary from case to case, as illustrated by the findings in congenital heart disease and haemolytic disease of the newborn. On the other hand, anoxia without cardiac stress, as seems to occur in cases of haemorrhage in the neonatal period, does not result in fatty change in the myocardium.

Possibly the fat is transported to the heart, but, owing to the extenuating circumstances, is not adequately metabolized and so becomes unmasked.

In hyaline membrane disease an interesting correlation existed between the amount of fatty change, the duration of life, and to a less extent the amount of membrane itself. There were four exceptions to this general rule, and it is possible that other factors, not necessarily cardio-respiratory in origin, may occasionally be responsible for membrane formation.

In almost a third of hyaline membrane cases the membrane is patchy and the babies live only a few hours. Death is really due to a primary atelectasis. It is very doubtful if these cases should be classified as hyaline membrane deaths.

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QUININE SENSITIVITY

BY

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AND

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Cinchonism, which is the name given to the symptom-complex of nausea, vomiting, disturbance of vision, tinnitus, and nerve deafness, may occur in any patient taking large doses of quinine (Goodman and Gilman, 1956). It is probably a physiological result of the high quinine content in the blood. When a patient who is taking only small doses of the drug develops the symptoms of cinchonism he is said to have an intolerance, or idiosyncrasy; there is no evidence that this is dependent upon an immunological mechanism (Pillsbury *et al.*, 1956).

A wide variety of dermatoses have been described in patients taking quinine systemically, and contact dermatitis may follow the topical application of quinine. These eruptions are thought to be based on an allergic process. Quinine, even in high concentration, has no irritant or direct toxic action on the skin. Although a large number of people have quinine-containing preparations applied to their skin as medications, scalp lotions, chemical contraceptives, or for other purposes, only a small number will develop an eruption: those who do so will nearly always show thereafter a positive patch test to dilute solutions of a quinine salt.

Eruptions ascribed to systemic administration of quinine are thought to be examples of allergic hypersensitivity because: (1) they are dissimilar to the effects of overdosage (cinchonism), (2) they may be provoked by extremely small doses of the drug, and (3) they occur only, and always, on re-exposure to the drug. In common with most instances of supposedly allergic drug reaction, skin tests by prick, scratch, intradermal, or patch technique are usually negative, unless the patient has been additionally sensitized by cutaneous contact.

We report here the details of five patients who developed a rash attributable to quinine, each of whom was positive to the patch test. Some of them also experienced systemic reactions.

Case Reports

Case 1.—A man aged 40 presented in 1955 with a rash of 10 weeks' duration on his arms, legs, and genitalia which was diagnosed clinically as lichen planus. He gave a previous history of a contact dermatitis of the penis after his wife's use of a contraceptive pessary containing quinine. Some time later he suffered an episode of an eruption on the genitalia, palms, and soles after the ingestion of quinine. His general practitioner suspected that the presenting rash was also due to quinine sensitivity, since it seemed to have begun after the patient's wife had again used a quinine-containing contraceptive pessary. A patch test to a 2% solution of quinine sulphate was positive after 48 hours.

Case 2.—A 25-year-old man presented in 1956 with an eczematous eruption of his perineum and genitalia which had been present for two months; it started after his wife had begun using a proprietary brand of a quinine-containing contraceptive pessary. Patch tests to the pessary and to a 2% solution of quinine sulphate were positive. Tests with 0.1% mercuric chloride and ammoniated mercury ointment were negative.

Case 3.—A man aged 31 was referred in 1957 by his general practitioner as a case of balanitis, possibly due to contact dermatitis. He had been using a rubber condom, and his wife may have been using chemical contraceptive pessaries. Positive patch tests were obtained with a piece of rubber from the condom, a quinine-containing pessary, and a 2% solution of quinine sulphate.

Case 4.—A man aged 36, whose occupation was a ladies' hairdresser, was first seen in May, 1953, with an acute dermatitis of the scalp, face, neck, and left hand of two weeks' duration. This had started on his bald scalp the day after he had used a proprietary brand of quinine-containing hair-restoring lotion; it resolved after one week's treatment in hospital. In the next few years he had several mild recurrences of dermatitis of the face and hands, and in 1957 he had a further acute attack necessitating admission to hospital. On this occasion a patch test with 2% quinine sulphate was positive, and the past history was obtained that at the age of 22 he had had an eruption on the genitalia after his wife's use of a chemical contraceptive containing quinine. In 1958 he again developed an acute dermatitis of the face and hands. This had begun on the day after he had had a tooth extracted, and, although none of the materials used by his dentist contained quinine, it is possible that the patient had taken a quinine-containing analgesic tablet.

Case 5.—A man aged 40 was seen in March, 1961, with a generalized itching, macular, erythematous eruption which was not scarlatiniform. He had recently had an entirely similar episode. Both attacks cleared up in three or four days. His previous history was that in childhood he had developed a scarlet-fever-like rash after taking a "tonic", he was subsequently told that he was sensitive to quinine. When aged 34 he had an acute dermatitis of the scalp after using a proprietary hair lotion (presumed to have contained quinine). Further inquiry then revealed that both episodes of the erythematous rash this year started on the day after he had drunk gin and "bitter lemon." A proprietary brand of the latter contains 3 mg. of quinine per 100 ml. Skin tests were done with 1% quinine sulphate in normal saline. The scratch and intradermal tests gave negative immediate-type reactions, but the patch test was strongly positive after 72 hours.

Discussion

The most common eruption caused by quinine is a generalized scarlatiniform rash, and Osler (1901) includes quinine rash in the differential diagnosis of scarlet fever. Although skin tests are not usually helpful in the diagnosis of drug allergy, there are isolated reports of positive skin reactions with quinine sensitivity. Boerner (1917), Dawson and Garbade (1930), Settle (1936), and Orr (1945) each described finding a positive immediate weal response to a scratch test with quinine in subjects sensitive to oral quinine. Settle's patient had a fixed drug eruption with bullae on the palms, and the scratch test itself provoked a focal flare.

In cases reported with a positive patch test to quinine a previous cutaneous contact with the drug had usually occurred (Kissmeyer, 1938; Bonnevie, 1939; Dold, quoted by Bonnevie, 1939). However, in 3 of the 20 patients described by Bonnevie no previous quinine contact was discovered. Bloch (1924) reported the case of a boy of 14 with atopic eczema who had a positive patch test to quinine, who had had no previous contact with quinine. A small dose (10 mg.) of quinine by

mouth produced an acute facial eruption, swelling of the fingers, and an attack of asthma 10 hours later.

Novy and Lamb (1957) described the case of a patient who presented at the age of 36 with a generalized dermatitis 24 hours after drinking a "few gin and tonics." He had had repeated eruptions since childhood, each caused either by the ingestion or application of quinine, and the whole pattern of his illness was very similar to that of one of our patients (Case 5).

Contact dermatitis from quinine is mentioned by Sulzberger (1940), by Becker and Obermayer (1947), and by Urbach and Gottlieb (1946). The last-mentioned authors published the photograph of a patient with an acute dermatitis of the face after using a hair lotion containing quinine.

Since 1938 quinine has been included in the standard series of patch tests applied to all patients with eczema at the Finsen Institute in Copenhagen. The incidence of positive reactions to quinine has steadily declined and are now distinctly rare (Hjorth, personal communication, 1961).

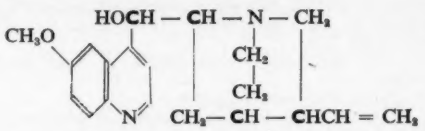
All of our five patients had positive patch tests and all gave a clinical history of a reaction after cutaneous contact with quinine. It is difficult to estimate whether quinine is a potent contact sensitizer or not, unless one can relate the incidence of reactions to the number of persons exposed to it. One would not regard it as a strong sensitizer when compared with penicillin, sulphonamides, or paraphenylenediamine; it is interesting to note, however, that contact sensitivity has been experimentally produced in guinea-pigs (an animal less prone to contact sensitivity than man) by the repeated topical application of quinine (Landsteiner and Chase, 1941).

More serious forms of adverse reaction to quinine are acute intravascular haemolysis and purpura. In the latter the platelet count may be low, and may be associated with a circulating antibody to the quinine-platelet complex (Ackroyd, 1958). This antibody can be demonstrated by an *in vitro* test similar to that used for detecting allergic thrombocytopenia from use of "sedormid."

Discombe (1958) states: "Quinine has long been notorious as a determinant of blackwater fever in patients with malignant tertian malaria . . . and in occasional patients who have never been exposed to malarial infection. Of these the most important group is pregnant women." This special susceptibility in pregnancy probably relates to the large single dose that may be taken for a reputed abortifacient effect, as in the fatal case reported by Vartan and Discombe (1940). Although the mechanism of this acute haemolysis is not known, observations made by Brost (1956) on two sisters with quinine purpura, one of whom had also had quinine-induced haemolysis, suggests that there may be a genetic factor which makes the patient's erythrocytes susceptible to destruction by quinine (Discombe, 1958). This may be of a similar nature to the glucose-6-phosphate dehydrogenase defect which is responsible for the lysis of ageing red cells by pamaquin and other drugs (*Brit. med. J.*, 1961).

Sources

Cinchona, the dried bark of the cinchona tree, contains a mixture of more than 20 alkaloids, the most important being two pairs of optical isomers: (1) L-quinine and D-quinidine, and (2) L-cinchonidine and D-cinchonine. The structural formula of quinine is:



the four asymmetric carbon atoms being marked in bold letters.

Quinine has now been largely replaced as a prophylactic against malaria, and is less popular as a constituent of "tonics" and simple analgesic and antipyretic mixtures—probably because it has been established to have only a weak antipyretic action, and to be no more effective than aspirin as an analgesic (Goodman and Gilman, 1956). Of the common proprietary analgesics only "anadin" contains quinine to the extent of 5 mg. in each tablet. The *Dental Formulary* contains an equivalent quinine-containing analgesic tablet, which is apparently widely prescribed by dentists (Hadgraft, personal communication, 1961) Quinine is still given orally to patients with myotonic conditions and non-specific night cramps.

Quinine is used in combination with an ion-exchange resin as quinine carbacrylic resin ("diagnex") as an oral tubeless test for gastric acid secretion. One of its soluble salts (0.003% w/v of quinine) is the "bitter" in "bitter lemon" and "tonic water." It may be encountered topically in proprietary hair lotions. Harry (1955) gives the prescription of a typical scalp lotion as 0.2% quinine in an alcoholic solution. It is employed in some chemical contraceptives for its spermicidal effect —for example, Rendall's contraceptive pessary contains 3.5% of quinine.

Summary and Conclusions

Five cases are described of patients who were proved by patch tests to have allergic contact sensitivity to quinine. Three of them presented with a contact dermatitis from quinine, and the others had had such episodes in the past. Three of the patients had experienced eruptions from systemic administration of quinine, and one reacted after drinking a proprietary brand of "bitter lemon." None of them gave positive scratch or intradermal tests to the drug.

The literature on quinine-induced skin eruptions, the toxic effects of quinine, and the role of skin tests in quinine sensitivity are briefly reviewed, and reference is made to the more common ways in which patients may encounter quinine.

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MENSTRUATION AND CRIME

BY

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It has been shown that during menstruation a deterioration occurs both in a schoolgirl's work and in her behaviour (Dalton, 1960a, 1960c), and it is also at this time that women are most liable to be involved in accidents (Dalton, 1960b) or to be admitted to hospital with an acute psychiatric illness (Dalton, 1959). This gradual recognition of the social significance of menstruation in the various aspects of a woman's life has led to an investigation of the importance of the menstrual factor in crime.

Over a period of six months in one of H.M. Prisons I interviewed all newly convicted women below the age of 55 on the first weekday after their sentence. The prisoners were asked their age, parity, duration of menstruation, length of cycle, date of last menstruation, and whether they observed any symptoms before or during menstruation. A similar interview was arranged for all prisoners who had been reported to the governor for bad behaviour while serving their sentence.

Results

Of the 386 newly convicted prisoners, 284 (74%) were menstruating regularly and 156 (41%) had committed their offence during the previous 28 days. Table I shows the distribution of the menstrual history of the newly convicted prisoners.

TABLE I.—*Menstrual History of* 386 *Criminal Women*

Regular menstruation		284
Offence committed within 28 days	156	
More than 28 days since offence	102	
Unable to recall date of last menses	26	
Amenorrhoea		38
Probably pubertal	6	
,, pregnant	28	
Puerperal	4	
Menopause		64
Natural	48	
Artificial	16	

In analysing the results, the method used was that described in previous surveys into the relationship of menstruation to acute psychiatric illness (Dalton, 1959) and accidents (Dalton, 1960b). The menstrual cycle was divided into seven four-day periods, in which Days 1–4 represented menstruation and Days 25–28 the premenstruum. The relationship of the date of offence to menstrual cycle in the 156 women who committed their offences during the previous 28 days is shown in Table II.

Nearly half of all crimes (49%) were committed by women during menstruation or in the premenstruum. On a normal distribution, only two-sevenths (29%) of all crimes would be expected during this period of eight days. The probability of a distribution, such as has been found, occurring by chance is less than one in a thousand ($\chi^2 = 12.7$ on 1 d.f.) and therefore suggests that the association between menstruation and crime is highly significant.

TABLE II.—*Time of Crime of* 156 *Regularly Menstruating Women*

Day of Cycle	No.	%
1–4	41	26·3
5–8	13	8·3
9–12	20	12·8
13–16	21	13·5
17–20	19	12·2
21–24	7	4·5
25–28	35	22·4
Total	156	100

Menstruation seems of greater importance in crimes of theft: 56% of such crimes occurred during menstruation and the premenstruum, whereas for prostitution the figure was 44% (Table III). Seven of the 13 (54%) alcoholics were sentenced at this time. "Theft" is used here to include all offences against another's property—for example, shoplifting, burglary, embezzlement, forgery. "Prostitution" covers those convicted under the Street Offences Act, 1959. "Alcoholism" covers those found drunk and disorderly in public places and refusing, or unable, to pay the fine. Menstruation is also of greater importance among first offenders than among those with more than three previous convictions. It was noted that nulliparous women were most liable to commit their offences during the premenstruum and the parous women during menstruation; this is similar to the difference in accident proneness among nulliparous and parous women (Dalton, 1960b).

TABLE III.—*Crimes Committed During Menstruation and Premenstruum*

Type	Crimes during Menstruation and Premenstruum		Total Crimes	χ^2 on 1 D.F.	Probability
	No.	%			
All crimes	76	48·7	156	30·9	<0·001
Theft	36	56·3	64	18·5	<0·001
Prostitution	34	43·6	78	8·6	<0·01
Alcoholism	7	53·8	13	*	*
First offence	21	51·2	41	10·3	<0·001
2nd and 3rd offences	25	49	51	10·4	<0·001
4 or more offences	19	47·5	40	7·0	<0·05

* Too few to determine probability.

The dates of conviction of those 102 women who menstruated regularly and whose crime had been committed more than 28 days previously were evenly distributed throughout the menstrual cycle. It would appear, therefore, that menstruation had no prejudicial effect on those women during their appearance in court.

"Premenstrual tension" was defined as mood changes, headaches, tiredness, bloatedness, or mastitis during the

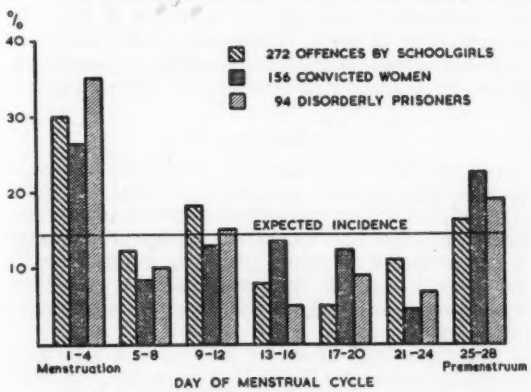
premenstruum, and "dysmenorrhoea" was defined as pain during menstruation. Premenstrual tension was present among 43 (27%) of the 156 prisoners whose offences had occurred during the previous menstrual cycle, and 27 (63%) of these 43 women had committed their crime during the time of their symptoms. Premenstrual tension was more common among those sentenced for theft (29%) than among the prostitutes (19%); in fact, the incidence of premenstrual tension among prostitutes is probably below that for women generally. Dysmenorrhoea was present in only 22 of the 156 prisoners (14%) who had committed their crime during the previous menstrual cycle, and these 22 prisoners had a normal distribution of crime throughout the menstrual cycle.

Among the prisoners reported for bad behaviour were 94 who were menstruating regularly, and 51 (54%) of these were disorderly during menstruation or the premenstruum. Among the 54 prisoners reported only once, 43% were associated with menstruation, whereas among the 40 prisoners reported more than once, 70% were associated with menstruation. This is similar to the observation among schoolgirls that the adverse effect of menstruation was greatest among those with most offences (Dalton, 1960c).

In cases where the reported prisoner suffered from premenstrual tension and had been disorderly during this time, the prisoner was offered the opportunity of treatment for premenstrual tension.

Discussion

The marked similarity of the effect of menstruation on naughty schoolgirls, newly convicted women, and disorderly prisoners is shown in the Chart. The offences



Times of offences during menstrual cycle.

for which the naughty schoolgirls were punished were petty and might be committed by any law-abiding citizen—for example, talking when silence is requested, lateness, forgetfulness—and would appear to be an altogether different type from those crimes for which a prison sentence is passed, or the offences for which a prisoner is reported to the governor. The hormonal changes of menstruation probably make the individual less amenable to discipline.

The analysis shows that there is a highly significant relationship between menstruation and crime. This could mean that the hormonal changes cause women to commit crime during menstruation and the premenstruum and/or that women are more liable to be detected in their criminal acts during this time. The adverse effect of menstruation was greatest among sufferers of premenstrual tension, with its concomitant symptoms of lethargy, slower reaction time, and mental dullness; and these factors would lead to easier detection during certain days of the menstrual cycle, especially among habitual law-breakers—for example, prostitutes and shoplifters. Premenstrual tension is also accompanied by irritability, lethargy, depression, and water retention, and these symptoms alone may be responsible for certain crimes—for example, irritability and loss of temper may lead to violence and assault, lethargy may lead to child neglect, and depression to suicide (still a crime at the time of investigation). If water retention is present in an alcoholic, then alcohol retention tends to occur, increasing the liability for the woman to become drunk and disorderly.

One alcoholic aged 45 years, with numerous previous sentences, described how she usually started menstruating during her stay in the police cell or first day in prison and also how alcohol had a more deleterious effect on her during this time, yet she sought solace in alcohol when she became depressed.

These findings again emphasize the need for a simple test for the presence of premenstrual tension. Unfortunately, the severity and type of symptom may vary from month to month and symptoms increase at times of stress, thereby adding to the difficulties of diagnosis. Premenstrual tension responds to treatment, but such treatment would need to be continued after the expiration of the prison sentence if any improvement in criminal tendency is to be expected; this suggests the need for such women being placed on probation subject to regular medical supervision.

Summary

An investigation carried out in a women's prison revealed that almost half the women committed their crime during menstruation or the premenstruum. Premenstrual tension appears to be an important factor, and 63% of the sufferers committed their crime at the time of their symptoms.

I wish to thank the Governor and members of the Prison Medical Service for their co-operation and helpful suggestions. This paper is published with permission of the Prison Commission though it does not necessarily represent their views.

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In order to help assess the suitability of background music for hospitals, the King Edward's Hospital Fund for London has undertaken to pay for trials in which six London hospitals are co-operating. For a period of six months background music will be provided in different areas in these hospitals, including an out-patient waiting-hall, casualty department, radiography waiting area, antenatal clinic, and a linen-room, as well as in male and female wards, where the continuous background music will be available through headphones for 24 hours a day, if required. The hospitals concerned have agreed to prepare reports on the trials at the end of six months.

Preliminary Communications

Reinforcing Doses of Diphtheria Toxoid Absorbed Through the Buccal Mucosa

Peroral administration of diphtheria toxoid for primary immunization and for reinforcing doses has been attempted previously. Bousfield (1945) gave volunteers two, three, or four gelatin disks to suck daily for seven days. Each disk contained about 100 Lf of diphtheria toxoid, so that the total amount of toxoid administered varied from 1,400 to 2,800 Lf. In most of the volunteers with a previous history of immunization or of an attack of diphtheria increases in antitoxin content occurred. Masucci *et al.* (1948) made similar studies using compressed tablets and confirmed Bousfield's finding. They suggested that three tablets should be given daily for seven days, a total of 2,100 Lf. Greenberg and Fleming (1950) gave volunteers large doses of toxoid by mouth, but in this case the toxoid was swallowed. These results were less satisfactory than those of Bousfield and of Masucci.

The administration of diphtheria toxoid without injections has attractions even if its use is limited to reinforcing immunity.

Hyaluronidase, which is almost completely non-toxic (Seifter, 1950), probably increases the rate of absorption of fluids through the mucous membranes by dissolving the hyaluronic acid, one of the components of the cement between cells. It has been used successfully in dental surgery to improve the absorption of local anaesthetics through the buccal mucosa (Trotter, 1954). In a preliminary study described below hyaluronidase and diphtheria toxoid, incorporated in lozenges which were held in the mouth until they dissolved, have been found to stimulate increases in antitoxin titres. An earlier unpublished study of lozenges without hyaluronidase gave equivocal results.

PRESENT INVESTIGATION

Preparation of Lozenges.—Each lozenge contained 1,500 Lf of purified diphtheria toxoid and 1,500 units of hyaluronidase. Two lots of lozenges were prepared. The lozenge base in lot A consisted of lactose, icing sugar, ethyl cellulose, and magnesium stearate. These lozenges were slow to dissolve; they remained in the mouth for about an hour before they finally disintegrated. Lot B was therefore prepared with a base of sorbitol, 100 mesh, 1,150 mg., and magnesium stearate 24 mg. per tablet. These lozenges dissolved in about 20 minutes.

Test Groups.—The test groups were composed of volunteers from members of the staff of the Central Public Health Laboratory, Colindale. Lot A was given to one test group and lot B to the other. A sample of blood was withdrawn from the volunteers before the study began. They were given two lozenges to suck, one immediately after the sample of blood had been taken and one a week later. Two weeks after the second lozenge a second sample of blood was taken.

Local and General Reactions.—No local or general reactions were observed in the volunteers.

Age Distribution and Previous History of Immunization.—The age distribution of the volunteers and their previous history of immunization are given in Table I. Forty persons took part in the study. Twenty-two had a definite history of previous immunization and 18 either were not previously immunized or were unable to say definitely whether they had been immunized. The ages of those given lozenges from lot A were on the average higher than those given lozenges from lot B; 9 of the 22 given lozenge A were 30 years of age or more, compared with 2 of the 18 given lozenge B. It was mainly among the older volunteers that the history of previous immunization was absent or indefinite.

TABLE I.—*Age Distribution and Immunization History*

Age in Years	History of Previous Immunization			
	Definite		Absent or Indefinite	
	Lozenge A	Lozenge B	Lozenge A	Lozenge B
15–	1	4	0	1
20–	6	9	6	2
30–	0	2	3	0
40–	0	0	4	0
50 and over	0	0	2	0
All ages	7	15	15	3

Antitoxin Titrations.—Antitoxin estimations were done on the paired samples of sera. The antitoxin was titrated by the intracutaneous injection of toxin/antitoxin mixtures into the flanks of depilated female guinea-pigs according to the method described by Römer (1909). Human serum titres were determined by correlating the results obtained in these tests with those given in similar tests with the international horse standard antitoxin. This was valid because curves plotted from results of neutralization tests of human sera from immunized people with toxin doses of Lr/1,000 and Lr/10,000 ran parallel with those obtained with the international horse standard antitoxin. Experiments were also done which showed that the Lr/1,000 and the Lr/10,000 doses of the international toxin were in each case 20 times the concentration of the Lr/1,000 dose of the toxin used in these experiments. This indicated that the combining-power in relation to the toxicity of both toxins ran parallel.

RESULTS

The results in volunteers with a definite history of previous immunization are shown in Table II, and in volunteers with no previous history, or with an indefinite history, in Table III. In Table II persons given lozenge A and lozenge B are shown separately, but in Table III this division has not been made because only three volunteers given lozenge B had no previous history of immunization.

The results with lozenge A and lozenge B in those previously immunized (Table II) were similar. In group

TABLE II.—*Antitoxin Titres in Persons with a Previous History of Immunization*

Test Group	Serum Sample	Antitoxin Titres (Units/ml.)						
		<0·001	≥0·001 <0·01	≥0·01 <0·1	≥0·1 <1·0	≥1·0 <10·0	≥10	Total
A	Pre-immunization ..	2	2	2	1	0	0	7
	Post-immunization ..	0	1	0	5	1	0	7
B	Pre-immunization ..	6	3	4	1	1	0	15
	Post-immunization ..	1	1	2	6	4	1	15
A+B	Pre-immunization ..	8	5	6	2	1	0	22
	Post-immunization ..	1	2	2	11	5	1	22

A=Group given the slowly disintegrating tablet. B=Group given the more rapidly disintegrating tablet.

A one of seven had an antitoxin titre of 0.1 unit or more per ml. before the tablets were given, and six of seven had 0.1 unit or more after the tablets were given. In group B 2 of 15 had 0.1 unit or more of antitoxin per ml. before the tablets were given and 11 of 15 had 0.1 unit or more per ml. after the tablets were given. In the two groups together, titres of 0.1 unit per ml. or more were observed in 3 of 22 sera before the tablets were given and in 17 of 22 afterwards.

In the group with a negative or indefinite history of previous immunization (Table III) 5 of 18 sera contained 0.1 unit or more of antitoxin per ml. before the tablets were given and 11 of 18 afterwards.

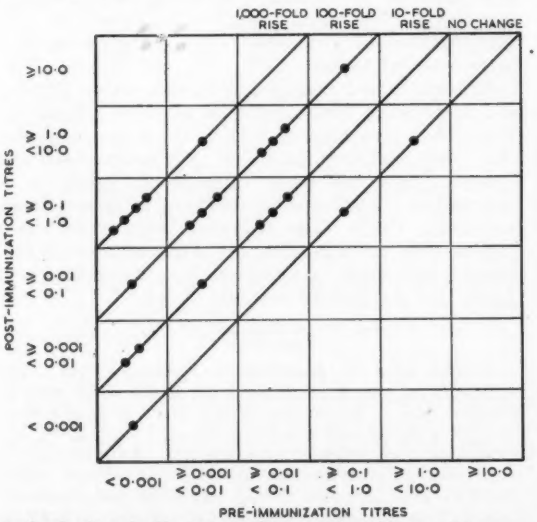
TABLE III.—*Antitoxin Titres in Persons with No* Previous History of Immunization*

	<0·001	≥0·001 <0·01	≥0·01 <0·1	≥0·1 <1·0	≥1·0 <10·0	≥10	Total
Pre-immunization	8	1	4	5			18
Post-immunization	1	3	3	5	3	3	18

* In some there was an indefinite history of immunization.

It is doubtful whether the results in Table III indicate that the lozenges would be effective in primary immunization. The volunteers concerned probably had either been previously immunized or been in contact with natural infection, and the increases in titre were the result of the response to a reinforcing dose.

The individual titres before and after the administration of the lozenges are shown in the Graph for the 22 volunteers with a previous history of immunization. Only one of eight subjects with less than 0.001 unit of antitoxin per ml. before the lozenges were given remained in this category afterwards. Of the others only two—one whose serum contained between 0.1 and 1 unit of antitoxin and the other whose serum contained between 1 and 10 units before the lozenges were given—failed to show a tenfold or greater increase in the antitoxin level after receiving the lozenges. Six showed tenfold increases, eight 100-fold increases, and five 1,000-fold increases.



Antitoxin titres in 22 persons with a previous history of immunization (groups A and B together).

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DISCUSSION

These preliminary results indicate that diphtheria toxoid can be absorbed through the buccal mucous membrane in quantities sufficient to stimulate a substantial antitoxin response in persons previously immunized. The increases observed are similar to those obtained by Edsall *et al.* (1954) after two injections each of 1 Lf of alum-absorbed toxoid given three weeks apart to young adults, but they are less than those obtained by the same workers when they gave a third dose, also of 1 Lf. However, of the 22 previously immunized subjects it is probable that only one would have been Schick-positive after the lozenges. The method is thought to be promising enough to warrant further large-scale studies, and these are now in progress in children aged 10–12 years in whom reinforcing immunization by the oral route would be of considerable practical value.

SUMMARY

In a preliminary study two lozenges each containing 1,500 Lf of purified diphtheria toxoid and 1,500 units of hyaluronidase were given a week apart to 40 adult volunteers to suck. An increase in antitoxin titre was observed in blood samples taken two weeks after the lozenges were administered. The results justify further study of the lozenges as a means of producing satisfactory antitoxin responses to reinforcing immunization in children primarily immunized by parenteral injections.

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Medical Memoranda

Finger-tip Necrosis in the Newly Born : a Hazard of Wearing Mittens

In recent years a disquieting number of therapeutic mishaps and nursing accidents involving neonates have come to light. Another form of avoidable injury results from the common practice of applying mittens† to the hands of newly born infants.

CASE 1

A prematurely born infant of 28 weeks' gestation and birth weight 2 lb. 13 oz. (1,275 g.) was admitted to the Royal Alexandra Hospital for Sick Children, Brighton, aged

†The mitten customarily used for neonates is a bag made of cotton material with a seam at the top and down one side. This accommodates the whole hand and the covering is secured at the infant's wrist with tapes or a drawstring.

4 days, because of hyperbilirubinaemia. Exchange transfusion was just avoided. Five and a half weeks later the baby was removed from an incubator and clothed for the first time. At this point cotton mittens were applied.

A few days later, after a feed which was taken well, the mittens were removed as a part of a change of clothing. On taking off the left one a piece of cotton from the interior of the top seam was found tightly wound round the middle finger in the region of the proximal interphalangeal joint and the distal part of the finger was black. After removing the offending thread the circulation slowly improved, but the next day the finger presented the ugly appearance shown in Fig. 1. In spite of prophylactic tetracycline the haemorrhagic bleb on the back of the finger became infected. Three weeks later a remarkable degree of recovery had occurred, but the whole finger was still swollen and there was obviously some loss of terminal pulp tissue. The nail had separated and there was a yellow crust in its place.

At the age of 15 months the nail was normal but the finger-tip was tapered owing to loss of pulp tissue. Although movements at the terminal joint were good, full extension of the distal phalanx was not possible.

CASE 2

The incident in this case actually occurred a year before the one just described but only came to light subsequently.

The accident happened at home after the mother's discharge from one of our maternity units. A 3-weeks-old baby (the mother's first, for which she had been waiting 14 years) was wearing home-made nylon-and-wool knitted mittens. On the day of the mishap the mother was in the process of removing the right mitten at bath-time when she noticed it could not be completely removed because a thread from the inner seam was tightly encircling the index finger at the distal interphalangeal joint and had to be cut loose. The terminal part of the digit was purple-black. As soon as the thread was cut the circulation improved. However, the nail separated in a few days and it was soon apparent that the finger-tip was gangrenous. Thereafter recovery was slow, and it was necessary for the baby to attend the orthopaedic clinic for three months' treatment. Fig. 2 shows the appearance of the finger at the age of 1 year. The distal portion is foreshortened and bulbous in shape and there is a flexion deformity similar to that in Case 1.

COMMENT

The mechanism whereby an internal thread from a mitten becomes wound round a finger is not difficult to understand. A similar thing may happen occasionally to a toe of a child or adult if there is a loose thread inside the top of a sock. In the case of a baby, flexion and extension movements of the fingers inside the spacious bag will encourage coiling of a piece of cotton round the digit with increasing constriction. It is remarkable that this process and the ischaemic complications which follow should cause neither pain nor discomfort.

Nowadays mittens are rarely used in our hospitals. If a baby is scratching its face or sucking its fingers and making them sore then swaddling with a shawl for a few days seems to be a reasonable and safe alternative measure for dealing with such situations. For those who cannot be persuaded to abandon the use of mittens in the light of these two accidents, the only advice that can be offered is that the coverings should have a firm French seam and they should be examined carefully for internal threads before each application.

I thank Mr. Austin Brown for permission to publish details of Case 2; and Mr. S. T. Higgins for his help with the photographs.

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FIG. 1

FIG. 2

FIG. 1.—Case 1. Discoloured appearance of middle finger of left hand on day after accident. Note haemorrhagic bleb over back of middle portion of digit. FIG. 2.—Case 2. Appearance of index finger of right hand one year after accident. Note bulbous tip and flexion deformity at distal joint.

Pyridoxine-responsive Anaemia

Hypochromic anaemia is usually the result of iron deficiency. It may, however, occur despite the presence of normal or increased amounts of iron. Thalassaemia is the most familiar example of such a refractory hypochromic anaemia. Harris *et al.* (1956) described the first case of a naturally occurring iron-refractory hypochromic anaemia which responded to the administration of pyridoxine. Nine further cases have been recorded (Maier, 1957; Foy and Kondi, 1958; Gehrmann, 1958; Bishop and Bethell, 1959; Verloop and Rademaker, 1960; Erslev *et al.*, 1960; Jones and Hutt, 1961; Dawson *et al.*, 1961). It has been suggested that the reported cases of pyridoxine-responsive anaemia show too much variation for them to be regarded as a homogeneous syndrome at present (Jones and Hutt, 1961). The following observations on a patient with an iron-refractory hypochromic anaemia which responded completely to treatment with pyridoxine are perhaps pertinent.

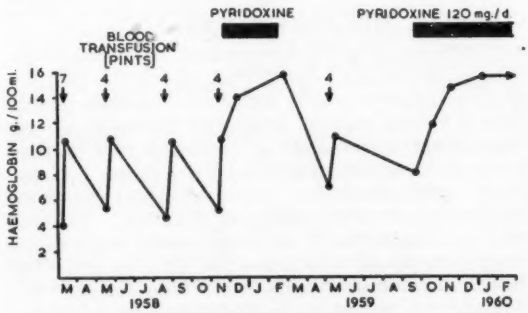
CASE REPORT

A man aged 61 presented in November, 1957, with symptoms of anaemia. Apart from pallor there were no physical signs of disease and he was found to have a hypochromic anaemia with a haemoglobin of 3.1 g./100 ml. The leucocytes and platelets were normal. A fractional test meal revealed complete achlorhydria, and tests of hepatic function were normal. No evidence of gastro-intestinal haemorrhage could be discovered and radiological examination of the small and large bowel was normal. There was no response to treatment with oral or parenteral iron and 6 pints (3.4 litres) of blood was transfused.

In March, 1958, he was severely anaemic again and required blood transfusion. The serum iron at this time was normal (110 μg./100 ml.). Isotope studies performed within three weeks of blood transfusion revealed a normal plasma iron turnover, and 80% of the ^{59}Fe had reappeared in the red cells by the ninth day. The survival of the patient's red cells labelled with ^{51}Cr was slightly reduced, the time taken for half disappearance being 21 days. He was given a further course of parenteral iron, but a recurrence of anaemia required blood transfusion in May and August.

In November the blood count was as follows: haemoglobin 5 g./100 ml.; haematocrit 24%; M.C.H.C. 21%; red-cell count 2,500,000/c.mm.; M.C.V. 94 cubic microns; reticulocytes 1%; leucocytes 7,700/c.mm.; platelets 290,000/c.mm. A blood film showed marked red-cell anisocytosis and moderate. poikilocytosis: the cells were very hypochromic and many target cells were seen. The patient's haemoglobin was electrophoretically normal and foetal haemoglobin was not increased (Dr. H. Lehmann). The osmotic resistance of the red cells was normal and Coombs test was negative. Aspiration of bone-marrow from the sternum provided films of increased cellularity; erythropoiesis was active and normoblastic, but the late normoblasts showed some deficiency of haemoglobinization. Staining of the bone-marrow for iron showed little increase in the amount of iron present. The serum iron was 266 μg./100 ml., which represented 100% saturation of the total serum-iron-binding capacity. The urinary urobilinogen was not increased and no porphobilinogen was detected in the urine. Family studies were limited to one daughter: her blood count and serum iron were normal and her haemoglobin was electrophoretically normal.

In November, 1958, after a blood transfusion had increased the haemoglobin to 10.1 g./100 ml., the patient was given pyridoxine 120 mg. daily. Within three weeks the haemoglobin had risen to 13.9 g./100 ml., and two months later it was 15.9 g./100 ml. He then stopped taking pyridoxine and within three months the haemoglobin had fallen to 7.3 g./100 ml. The serum iron at this time was 185 μg./100 ml. He was given a blood transfusion at another hospital, where it was not known that he had been treated with pyridoxine, but within another four months he was anaemic. He was again treated with pyridoxine 120 mg. daily and the haemoglobin rose from 8.6 to 15.8 g./100 ml. He has remained well and haematologically normal on pyridoxine therapy over the subsequent two years.



Course and treatment of case.

DISCUSSION

The hypochromic anaemia in this patient was at first thought to be the result of gastro-intestinal bleeding. No evidence of blood loss could be discovered and the high serum-iron level excluded iron deficiency as the cause of the anaemia. The response to pyridoxine was complete, and a normal haemoglobin level has been maintained for two years on 120 mg. of pyridoxine daily. There was no evidence of any dietary deficiency or of malabsorption. The normal ^{59}Fe turnover three weeks after a blood transfusion is of interest, as remissions of pyridoxine-responsive anaemia have been reported after the administration of whole blood or plasma (Erslev *et al.*, 1960). This observation is stressed, as unawareness of the fact may lead to an erroneous diagnosis of iron deficiency.

The association of haemochromatosis with some cases of pyridoxine-responsive anaemia (Maier, 1957; Bishop and Bethell, 1959; Verloop and Rademaker, 1960) has raised the problem of whether the anaemia precedes or follows the haemochromatosis. Bishop and Bethell (1959) have suggested that the excessive iron stores may impair haem synthesis: that this may in fact be true is supported by the observations of Crosby and Sheehy (1960), who demonstrated a fourfold increase in bone-marrow function in a patient with "iron-loading anaemia" who was subjected to repeated phlebotomies. However, when our patient presented with anaemia the serum iron was normal and there was no evidence of any significant increase in the bone-marrow iron, so that it is unlikely that excessive iron stores contributed to the pathogenesis of the anaemia. It may, however, be relevant to those reported cases in which the response to pyridoxine therapy was incomplete.

The differential diagnosis of pyridoxine-responsive anaemia includes thalassaemia and the less common forms of refractory hypochromic anaemia described by Rundles and Falls (1946), Mills and Lucia (1949), and Garby *et al.* (1957). These latter anaemias have been attributed to defects in haemoglobin synthesis and are often familial. One of the cases described by Rundles and Falls (1946) has since been shown to respond to pyridoxine (Bishop and Bethell, 1959). Thalassaemia cannot definitely be excluded in others, and as this disorder is now recognized in families of English stock (Havard *et al.*, 1958; Callender *et al.*, 1961) it becomes the principal differential diagnosis.

I thank Dr. R. Sleigh Johnson for referring this patient and for permission to report the clinical details.

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At its first annual meeting the Medical Committee against Racial Discrimination in South Africa reported that the year's activities had included a delegation to the South African High Commissioner to protest at the detention of twelve colleagues without charge or trial; the printing of a leaflet on how apartheid affects doctors, nurses, and medical teaching, and its circulation to some 8,000 members of the profession; and a drive to secure places and funds to enable 12 non-white South African medical students to study in the United Kingdom. The Secretary is Dr. ELEANOR ETTLINGER, 20 Lansdowne Crescent, London W.11.

Reviews

PROBLEMS OF TRANSPLANTATION

The Transplantation of Tissues and Organs. By Michael F. A. Woodruff, M.D., M.S.(Melb.), F.R.C.S., F.R.C.S.E., F.R.A.C.S. (Pp. 777+xxxiii; illustrated. £10 4s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Surgery has advanced to the stage where it is possible to transplant organs such as lungs, kidneys, the liver, or even the heart, from one subject to another. These transplantations are, however, at present successful merely on a mechanical basis, for the receiving organism soon produces an immunity reaction which destroys the grafted tissues after an initial period of successful function. Could this immunity rejection reaction be overcome surgery would make an advance comparable to that after Lister's introduction of antisepsis or the discovery of drugs for general anaesthesia.

It is natural, therefore, to find that the innumerable different aspects of this problem should be under study in medical centres everywhere. Work on some aspect of the problem of transplantation is going on in almost every university department of surgery where research is pursued, as well as in physiological and other laboratories. Professor Woodruff's encyclopaedic work will be of immense help to these workers, for it contains reviews and references to all this fundamentally important work.

It is, however, of even greater use, for it deals also with the practical application of methods of grafting tissues which are already of established value in clinical surgery. The author has had help from others in a few places—N. W. Nisbet collaborating in the section on transplantation of bone and G. T. Scott writing that on cornea—but most of the task of reviewing and describing the vast field has been done by the author himself. This gives the book the advantages in general clarity and readability of a one-author work, which is rare nowadays. It is difficult to praise it too highly.

J. B. KINMONTH.

BEST AND TAYLOR'S SEVENTH

The Physiological Basis of Medical Practice. Edited by Charles Herbert Best, C.B.E., M.A., M.D., D.Sc.(Lond.), F.R.C.S., F.R.C.P.(Canada), and Norman Burke Taylor, V.D., M.D., F.R.S.(Canada), F.R.C.S.Ed., F.R.C.P.(Canada), M.R.C.S.(Eng.), L.R.C.P.(Lond.). Seventh edition. (Pp. 1,554+xvi; illustrated. £6 8s.) London: Baillière, Tindall and Cox, Ltd. 1961.

The aplastic anaemia that seemed to be threatening the last edition of Best and Taylor has, one is relieved to find, not materialized. In retrospect the anaemia was due to simple iron deficiency secondary to an inadequate dietary intake. Very effective therapeutic measures have restored the haemoglobin level to normal in this new edition, and the prognosis is extremely good.

The authors must be congratulated on their successful therapy, which has consisted mainly of co-opting 28 erudite contributors from Canada, the United States, and Great Britain, the English physiologists being F. W. Campbell, B. T. Donovan, G. W. Harris, Sir Bryan Matthews, and E. N. Willmer—a tribute to the Cambridge school of physiology. The result has been that almost the whole book has been either rewritten or extensively revised. It is now an outstanding, up-to-date work, written in such good English that it is a pleasure to read and easy to comprehend. Even such difficult subjects as acid–base balance and hydrogen-ion concentration, which generations of medical students have despaired of understanding, are readily assimilated.

This book, as indicated by its title, is directed more towards medical men than pure physiologists, and hence it is important that whenever possible it should relate to human rather than animal physiology. Recent advances have repeatedly shown the danger of extrapolating from animals to man, and the increasing physiological studies made in hospitals and the physiological experiments induced by disease—experiments which could never be reproduced in the laboratory—make it less and less necessary in certain fields to rely on information derived from rats, dogs, and cats. Thus some of the best chapters in this book have been written by physiologists engaged in clinical work, and some of the chapters written by the predominantly animal physiologists are rather weak in their clinical aspects. Though it may be invidious to call attention to any particular section it would be ungracious not to mention the outstanding chapters on the circulation, largely written by Donald E. Gregg, and on the kidney, by Robert W. Berliner.

In a volume of 1,570 pages with 588 figures some typographical errors are bound to creep in (Simmond's repeatedly for Simmonds's disease, for example), but these are few. Perhaps in the next edition some new illustrations could replace the rather dated and indistinct blocks reproduced in the endocrine section. But these are small points, which in no way detract from an outstanding book.

R. I. S. BAYLISS.

THE HEALTHY CHILD

The Healthy Child. His Physical, Psychological, and Social Development. Edited by Harold C. Stuart and Dane G. Prugh. (Pp. 507+xvi. 80s.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1960.

This is a large volume, written by Harold Stuart and Dane Prugh with the aid of 20 contributors from the fields of paediatrics, psychology, psychiatry, nutrition, social work, obstetrics, neuropathology, preventive medicine, and public health and education. The book originated as a series of lectures on growth and development given by the Department of Maternal and Child Health of the Harvard School of Public Health. It is designed to provide a sound background knowledge of the normal child for workers in education, psychology, nutrition, social work, nursing, public health, and medicine. It includes chapters on the principles of growth and development; the physiology of childbirth; foetal malformations; maternal nutrition; the psychological implications of pregnancy; physical, psychological, and intellectual growth at various age periods, including adolescence; infant feeding; physical and psychological aspects of adolescence; and the function of the family.

I think that this book fully achieves its avowed aims. It is altogether desirable that the importance of knowledge of what is normal in children is becoming increasingly recognized, and this book gives a good and comprehensive—but not too advanced—account of the subject which will greatly help workers in many fields. I believe that all teachers would profit from this book, and workers in many other fields concerned with children, such as paediatricians and family doctors. It is not a book to which one would refer for the treatment

of specific problems, such as those of defective physical growth, the treatment of behaviour problems, the diagnosis of feeding difficulties, and other clinical matters, but it does give the background necessary for the understanding of many of these problems. The book can be heartily recommended.

R. S. ILLINGWORTH.

PREMATURITY

The Premature Baby. By V. Mary Crosse, O.B.E., M.D. (Lond.), D.P.H., M.M.S.A., D.Obst.R.C.O.G. Fifth edition. (Pp. 266+viii; illustrated. 24s.) London: J. and A. Churchill Ltd. 1961.

This book first appeared in 1945, and would never have seen the light of day had it not been for Dr. Crosse's courage and determination during those trying years when Birmingham, like other large cities, was subjected to bombing. It has rightly enjoyed much success, and the present edition, the fifth, will extend and increase its usefulness. A full revision has been carried out, some of the sections have been completely re-written, and additions have been made to the long list of references quoted at the end of each chapter. It is a common-sense book embodying the results of Dr. Crosse's vast experience of premature babies, and its practical approach to the subject is commendable. All the common problems are dealt with fully and some mention is made of most of the less common.

The general pattern remains as before. There are successive chapters dealing with definition, management and care, hospital care, home care, clothing, feeding, and complications. The last chapter includes much more than its title, "Prevention of Mortality Due to Prematurity," suggests, and it is especially useful for its careful evaluation of statistical evidence bearing upon many aspects of the problem of prematurity. It also gives a valuable assessment of the vexed question of prognosis. An appendix presents statistics from the Sorrento Maternity Hospital and its premature-baby unit.

The criticisms that can be made are relatively minor ones. It would be a help, particularly to the less experienced reader, if clinical descriptions were more carefully defined—for example, the word "poor" is used frequently and often means "in comparison with the function (or structure, or whatever it may be) in a mature child," but it sometimes stands for "impaired even for a premature baby." The section on intracranial birth injury (p. 125) lays too much stress on haemorrhage as one of the pathological results. The technique of obtaining a specimen of urine might usefully be described, either on p. 7 or p. 141.

This is an excellent book which should be available to all doctors attending premature babies.

N. B. CAPON.

SUBJECTIVE RESPONSES

Measurement of Subjective Responses. Quantitative Effects of Drugs. By Henry K. Beecher, M.D. (Pp. 494+xvi. £5 2s.) New York and London: Oxford University Press. 1960.

Between psychophysics, which is concerned with the measurement of subjective mental states, and "psychopharmacology," which examines the effects of drugs on mental states, the overlap is so obvious that those working in these two areas might be expected to be very familiar with the techniques and methods common to both. This has not always been the case. The group of investigators in Professor Beecher's department at Massachusetts General Hospital has, however, been sophisticated in this respect, and his book describes how it has concentrated on quantitative treatment of the introspective data provided by patients who are in pain. The study of pain and the effect of analgesics led the group on to investigate other forms of perception which could be modified by drugs.

In psychophysics from the time of Fechner emphasis has been laid on the relation between stimulus and sensation, or rather between stimulus and perception. Beecher holds that no constancy can be expected in that relation because individual reaction can vary so much, and that the assumption of a constant relation has led to much wasted effort. In accordance with his conviction on this score he deprecates the use of artificially induced pain in experiments, and devotes much space to a rather vehement polemic against Hardy, Goodell, and Wolff for their well-known and original investigations in which radiant heat was the pain-stimulus. He makes no reference to some significant studies, such as that of Birren, Casperson, and Botwinnik, which bear on his argument.

The first part of the book deals fully with the measurement of pain. It includes a valuable chapter by Professor Mosteller on the statistical problems and pitfalls in this field. The second part extends the application of Professor Beecher's method to the measurement of anxiety, hunger, nausea, euphoria, itching, and other subjective states. Psychotomimetic drugs are also considered.

This book is a record of sustained effort in a complex area of inquiry. Though the author is hardly judicial in appraising work which he thinks misguided, he has set out in readable and candid form an illuminating story of resourceful and energetic research.

AUBREY LEWIS.

PHYSICAL TREATMENT IN PSYCHIATRY

Somatic Treatments in Psychiatry. Pharmacotherapy; Convulsive, Insulin, Surgical, Other Methods. By Lothar B. Kalinowsky, M.D., and Paul H. Hoch, M.D. In collaboration with Brenda Grant, M.D., D.P.M. (Pp. 413+x. $9.75.) New York and London: Grune and Stratton. 1961.

Before the second world war the idea of a book devoted solely to physical treatments in psychiatry would have seemed little short of fantasy to the philosophically minded psychiatrists of the period. However, this book, the successor to an earlier one published by the same authors in 1946, shows the tremendous progress that has been made in this particular approach to the treatment of the mentally ill. And it is the full implementation of these physical methods of treatment in Great Britain that has also made possible so much of the progress along other lines in recent years, including the good use made of the new Mental Health Act.

This book, therefore, is bound to be of the greatest importance. Like its predecessor it is perhaps too much a reference book to other people's published work and opinions, with too little guidance given from the authors' own wide experience of treatment. Help on the choice of method and its selective indications is still very important to the younger psychiatrist and the practitioner, since the strong feelings for and against physical treatments in psychiatry have unfortunately produced many emotionally toned and conflicting viewpoints. The inexperienced reader may still get confused when he studies this book's sometimes too unselective

references to the literature on this subject. The fifty pages of closely packed references indicate both the great progress and the confusion still prevailing in this field.

On a few points, however, the authors were somewhat dogmatic in the past, and in this new book have performed something of a *volte-face*. For years, for instance, they continued to doubt that insulin coma was a better treatment for schizophrenia than the use of intensive electrical convulsive treatment alone. Now, however, much too late, they have rushed to the rescue of insulin coma just when its value has been greatly minimized by the advent of the tranquillizing drugs, which make the use of E.C.T. so much more effective in the treatment of this illness than it was in the past. In the face of the main body of orthodox American opinion at the present time, they do, however, make the sensible plea that the benefits of the new modified leucotomy techniques should not be forgotten, for the effect of the tranquillizers is sometimes only to quieten patients and make them more comfortable in hospital, rather than get them out of hospital and back to work. The chapters on the new tranquillizing and anti-depressant drugs are very informative and valuable.

WILLIAM SARGANT.

NAVAL MEDICINE

Medicine and the Navy, 1200–1900. Volume III—1714–1815. By Christopher Lloyd, F.R.Hist.S., and Jack L. S. Coulter, F.R.C.S. With a foreword by Surgeon Vice-Admiral Sir Cyril May, K.B.E., C.B., *M.C.*, F.R.C.S. (Pp. 402+xi; illustrated. 50s.) Edinburgh and London: E. and S. Livingstone Ltd. 1961.

In a review of the second volume of *Medicine and the Navy* the hope was expressed that the Naval Medical Service might find a worthy successor to that gifted historian Surgeon Commander Keevil. Thanks to the generosity of the Wellcome Trustees two men, well qualified to undertake the work, were entrusted with the onerous task of completing this history, which started so auspiciously under his brilliant pen. "You can never tell till you try" must have expressed the feelings of these two gentlemen when they undertook to continue Commander Keevil's work. However, the choice of Mr. Christopher Lloyd and Surgeon-Captain Coulter could scarcely have been bettered. Not only have they tried to emulate the accuracy and descriptive powers of the original author but they have succeeded in their task in a most remarkable way.

They rightly chose to alter the format of the original volumes somewhat. Volume III, a mighty tome of some 400 pages, is full of interesting details of the growth and development not only of the Naval Medical Service but also of medicine itself.

If this volume does nothing else it brings out the immense debt that the Royal Navy—and indeed Great Britain—owes to men like Lind, Trotter, Robertson, and Blane for their efforts in controlling scurvy, typhus, and yellow fever. The little table of diseases on page 371 is an eloquent testimony to their persistence and hard work.

Though the story is lengthy I felt no urge to "skip" such a thoroughly well-balanced tale, and the joint authors are to be congratulated on giving us a very readable, accurate, and interesting account, which is rightly named *Medicine and the Navy*.

J. C. A. DOWSE.

ENDOCRINOLOGY ANNUAL

The Year Book of Endocrinology. (1960–1961 Year Book Series.) Edited by Gilbert S. Gordan, M.D., Ph.D., F.A.C.P. (Pp. 408; illustrated. 60s.) Chicago: Year Book Medical Publishers Inc. London: Interscience Publishers Ltd. 1961.

Hard-pressed physicians fighting against impossible odds to remain cognizant of the rapid advances in endocrinology have in the past found this yearbook a splendid help. The new volume lives up to the high reputation of its predecessors.

To review it in detail is impossible, and to single out individual contributions for special mention would be unjustly invidious. It may, nevertheless, be fair to single out the fact that many of the contributions were presented at the First International Congress of Endocrinology in Copenhagen and at the Fourth International Goitre Conference in London—meetings which made 1960 a remarkable year for endocrinologists, both meetings being marked in Dr. Gordan's words "by superb preparation, the convening of the most distinguished and productive people in the fields."

The volume contains a special article by Baránov and his colleagues on advances made in Russia, and one by Costa (Turin) on cretinism. Apart altogether from the value of these special articles they are important contributions in that they herald a world-wide view which has not always been characteristic of American writers.

RAYMOND GREENE.

MICROCIRCULATION

European Conference on Microcirculation. Edited by H. Harders. (Pp. 426+x; illustrated. Sw. Fr. 65.) Basel, New York: S. Karger. 1961.

This is a collection of the papers presented at the European conference on microcirculation held at Hamburg in 1960. There are 53 papers, 29 in German, 23 in English, and one in French. All have German and English summaries. They vary in length from a single page to 15 or so, but most are very short.

The main subject is anatomy and fine structure. Several papers outline recent techniques—for example, observations on the circulation of rabbit's bone *in vivo*, "electronic image processing" for the study of choroidal blood vessels, television (microcinematography for observing the circulation in human conjunctival blood vessels), observations on the middle-ear vessels of the guinea-pig, and many articles on capillary microscopy in the skin and nail-beds.

There are a few articles of clinical interest: Oscar Gilje (Oslo) discusses the application of capillary microscopy to dermatology, P. G. H. J. Bosley (Warwick) illustrates the pathology of nail-bed capillaries in human subjects, and there are a few papers on the effect of "large fat meals" on small-vessel circulation.

The appendix is a review by Melvin H. Knisely on the settling of sludge during life, a subject in which he and his co-workers have been interested for 15 years or so, illustrated by studies on the circulation of monkeys infected with Knowlesi malaria.

This volume is well produced with stiff paper backs. The illustrations, including two colour plates, are excellent. But most of the material of value in a collection like this has been or will be published in the normal journals in greater detail. Its interest is there-

fore mainly for those who attended the conference. It can hardly be said to be worth over £5 of anyone else's money.

M. C. G. ISRAËLS.

BULGARIAN YEARBOOK

Bulletin de l'Institut de Médecine Expérimentale. Volume III. (Pp. 275; illustrated. No price.) Bulgaria: Edition de l'Académie des Sciences de Bulgarie. 1960.

The work under review is the yearbook for 1960 of the Division of Biological and Medical Science of the Institute of Experimental Medicine of the Bulgarian Academy of Sciences. It contains 19 papers in Bulgarian and Russian, with summaries in English, Russian, French, and German. Many are predominantly theoretical in content and only those communications of more clinical interest will be mentioned here.

Among these is a paper by A. Hranova on the effect of glutamic acid upon higher nervous activity in rats, in which it is shown that conditioned reflexes to sound and light—which had begun to diminish from lack of maintenance—could be restored by the administration of glutamic acid in the diet. D. Daskalov and co-workers have employed the electrophoretic dermogram, a method involving electrophoretic introduction of adrenaline and acetylcholine into the skin, in a study of the effect of intravenously administered ascorbic acid on autonomic reactivity. L. Glavcheva has investigated the effect of chlorpromazine upon gastric secretion in dogs, using the Pavlov-pouch technique. Given in doses of 1 to 2 mg. per kg. the drug inhibits the secretion of gastric juice, and the effect is probably mediated by the parasympathetic system and may also be due to a direct effect upon the secretory cells. Other papers deal with the structure-activity relationships of derivatives of ephedrine.

D. J. BAUER.

LUPUS VULGARIS IN DENMARK

Lupus Vulgaris Cutis in Denmark, 1895–1954. Its Relation to the Epidemiology of Other Forms of Tuberculosis. By Ole Horwitz. (Pp. 142; illustrated. $6.50.) Copenhagen. 1960.

The author has devoted five years to an exhaustive survey on a statistical basis of the problem of lupus vulgaris in Denmark. It is based on the work of the Finsen Institute in Copenhagen from 1895 to 1954.

An appendix comprising nearly half the book consists of 76 tables of figures. They deal with age of onset; age of admission; associated diseases; occupation and social status; relative activity of disease and cure; type of organism; mortality rates; and all combinations of these figures. The earlier chapters of this work indicate the methods employed in arriving at these figures and the aspects of the problem investigated. It may interest the statistician but will not excite the clinician, though it may have some value to those engaged in that field of study.

The factors of climate, nutrition, and the influences of stressful circumstances are not considered. It would have been helpful to have known something of the incidence of cancer among patients with lupus treated by *x* rays and among those not so treated, but this is not covered. The book does not add significantly to our knowledge of the subject.

J. T. INGRAM.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Lecture Notes on Pharmacology. By J. H. Burn, M.D., F.R.S. Sixth edition. (Pp. 143+viii. 8s. 6d.) Oxford: Blackwell Scientific Publications. 1961.

The Conquest of Baldness. The Wonderful Story of Hair. By Gilles Lambert. (Pp. 160; illustrated. 18s.) London: Souvenir Press. 1961.

Fit at Forty and After. By Oscar Heidenstam. (Pp. 141; illustrated. 16s.) London: Faber and Faber. 1961.

The Self and Others. Further Studies in Sanity and Madness. By R. D. Laing. (Pp. 186+ix. 25s.) London: Tavistock Publications. 1961.

Memorandum on Immunological Procedures. Which Service Personnel and their Families may Need at Home and Abroad. Issued by the War Office. (Pp. 79. 4s. 6d.) London: H.M. Stationery Office. 1961.

Functional Closure of Exstrophy of the Bladder. International Inquiry. By Victor F. Marshall and Franco de Gironcoli. (Pp. 52; illustrated. $2.) Treviso: Edizioni di "Urologia," Libreria Editrice Canova. 1961.

Some Observation on Cyclopropane Anaesthesia in Animals using a Portable Closed Circuit Apparatus, with Special Reference to Conditions in Central Africa. By Alan G. Warren, B.Sc. (Lond.), M.R.C.V.S. (Pp. 79; illustrated. No price.) London: Harrison and Sons. 1961.

Vision of the Aging Patient. An Optometric Symposium. Edited by Monroe J. Hirsch, O.D., Ph.D., and Ralph E. Wick, O.D. (Pp. 328+xviii; illustrated. 52s. 6d.) London: Hammond, Hammond and Co. 1961.

On Modern Physics. By Werner Heisenberg, Max Born, Erwin Schrödinger, and Pierre Auger. (Pp. 108. 18s.) London: Orion Press. 1961.

Hypnotism and the Supernormal. By Simeon Edmunds. (Pp. 180+xi. 25s.) London: Aquarian Press. 1961.

Medical Physiology. Edited by Philip Bard. Eleventh edition. (Pp. 1,339; illustrated. £6 3s. 6d.) St. Louis: C.V. Mosby Company. London: Henry Kimpton. 1961.

Appraisal of Current Concept in Anesthesiology. Edited and assembled by John Adriani, M.D. (Pp. 279. 58s.) St. Louis: C.V. Mosby Company. London: Henry Kimpton. 1961.

Lectures on the Methodology of Clinical Research. By Max Hamilton, M.D., D.P.M. (Pp. 139+viii. 21s.) Edinburgh and London: E. and S. Livingstone. 1961.

Psychology for Nurses. By Jennifer M. Jarvis, B.A., Dip.Psych., and John Gibson, M.D., D.P.M. (Pp. 131. 15s.) Oxford: Blackwell Scientific Publications. 1961.

Gravitational Stress in Aerospace Medicine. By Otto H. Gauer, M.D., and George D. Zuidema, M.D. (Pp. 278+xvi; illustrated. 97s. 6d.) London: J. and A. Churchill. 1961.

Surgery. A Concise Guide to Clinical Practice. Edited by George L. Nardi, M.D., and George D. Zuidema, M.D. By 23 authors. Foreword by Edward D. Churchill, M.D. (Pp. 1,033; illustrated. 60s.) London: J. and A. Churchill. 1961.

Manual of Refraction. By Albert E. Sloane, M.D. (Pp. 171; illustrated. 45s.) London: J. and A. Churchill. 1961.

Stedman's Medical Dictionary. Prepared by 23 Consulting Editors and 34 Associate Editors. 20th edition. (Pp. 1,680+xlvii; illustrated. £5 10s.) London: Baillière, Tindall and Cox. 1961.

Abdominal Surgery. By 41 authors. Editors: Arthur W. Allen, M.D., and David Woolfolk Barrow, M.D. Foreword by Frederick A. Coller, M.D. (Pp. 658+xiii; illustrated. £9.) New York: Paul B. Hoeber, Inc. London: Pitman Medical Publishing Co. Ltd. 1961.

The Merck Manual of Diagnosis and Therapy. Edited by Charles E. Lyght, M.D. Tenth edition. (Pp. 1,907. 60s.) Merck Sharp and Dohme Research Laboratories. 1961.

Clinical Aspects of Nuclear Medicine. Symposium with Special Reference to Cancer and Cardiovascular Diseases. By Lee E. Farr, H. W. Knipping, and William H. Lewis, in co-operation with R. W. Felten and H. Ludes. (Pp. 486; illustrated. DM. 49.) Köln and Upladen: Westdeutscher Verlag. 1961.

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PREVALENCE OF ANAEMIA

Anaemia, usually iron-deficiency anaemia, is often said to be one of the commonest diseases that the general practitioner has to deal with. Six years ago D. G. French[1] working in the Potteries reported that he saw 40 to 50 new cases of anaemia every year, most of them iron-deficiency anaemia. If such a figure is typical every general practitioner needs to be on the watch for anaemia as a possible cause of a patient's symptoms. For in few diseases is it so relatively easy to separate those patients who are readily treatable by simple means from those who must be more fully investigated before a firm diagnosis can be reached.

Two papers in the *Journal* this week present evidence that supports French's estimate of the prevalence of anaemia, but the evidence was gathered in a different way by each author. Dr. John Fry reports (page 1732) the anaemic cases that were found in his practice of 5,000 patients in south London over a five-year period. His patients were investigated only if they presented clinical signs of anaemia. That this is an efficient criterion is shown by the fact that 86% of the patients investigated on this criterion proved to have anaemia—that is, their haemoglobin level was less than 80% (100% = 14.8 g./100 ml. blood). He excluded pregnant patients and those in whom anaemia developed in the later stages of already established diseases. He found 433 patients with anaemia of all types, an annual incidence of 17.5 per 1,000; he points out that "this means that the average family doctor with a list of 2,500 may expect to meet some 52 patients with anaemia each year." Dr. G. S. Kilpatrick reports (page 1736) that he investigated the population of an area in Wensleydale, Yorkshire, and took blood samples from everyone; no clinical assessment was made. The haemoglobin content, the packed-cell volume, the mean corpuscular haemoglobin concentration (M.C.H.C.), and the serum iron were determined for each sample. Men with a haemoglobin level of 12.5 g./100 ml. (85%) and women with 12.0 g./100 ml. (81%) or less were classed as anaemic. Out of 182 men 14 (7.7%) were thus found to have anaemia, and out of 230 women 48 (21%) were anaemic, a total incidence of 15%.

If anaemia is so prevalent what are the clinical signs and symptoms that suggest to the practitioner that investigation will be worth while? The classical symptoms are increasing and undue fatigue after tasks normally undertaken without discomfort, dyspnoea and palpitation after moderate exertion, and sometimes swelling of the ankles, especially in the evenings; soreness of the tongue and flatulent indigestion may also occur. On examination the conjunctivae will be pale, the tongue may be smooth, the nails spoon-shaped, and the pulse rapid. However obvious the anaemia, it is essential that a full physical examination should be carried out to elucidate its cause. Palpation for instance may disclose a tumour in the gastric region or an enlarged spleen. In practice only a minority of patients show clear signs and symptoms of anaemia, and it is remarkable how low the haemoglobin level can fall before the patient seeks advice.

If anaemia is suspected the next step is to confirm the diagnosis by examination of the blood. Dr. Fry does this by sending the patient to the local laboratory for a blood count, and this is the best way. But many practitioners are not so favourably placed; the trip to the nearest laboratory may be long and awkward. Here the doctor who can carry out his own haemoglobin estimations can save much time and trouble. Reliable simple methods are available: the Haldane haemoglobinometer made to British Standard specification is inexpensive and easy to use; the M.R.C. grey-wedge photometer can be used with oxyhaemoglobin, so no carbon monoxide is needed, and it too is reliable. The Sahli acid-haematin method now uses a similar standard to the Haldane haemoglobinometer, but has the disadvantage that the solution must stand for half an hour or so before reading. Tallqvist's papers are too inaccurate and should not be used.

When the fact of anaemia is established, what then? It is certainly unnecessary to send every patient to hospital for examination; the largest group of patients with anaemia, women in the reproductive period of life, have most frequently an iron-deficiency anaemia without serious underlying disease. Fry reports a 4:1 ratio of females to males in his cases; iron-deficiency accounted for 92% of all cases, and in 83% of the female patients with iron deficiency no serious underlying disease was found. If a full blood count is available cases of anaemia other than those due to iron deficiency will be detected at once. But if

[1] French, D. G., *Proc. roy. Soc. Med.*, 1955, **48**, 347.
[2] See *Brit. med. J.*, 1959, **2**, 812.

the haemoglobin level only is known it is safe for the practitioner to give iron preparations to this group of women and to watch the results, provided that the physical examination fits in and, for example, there are no signs pointing to the possible existence of malignancy or of a megaloblastic anaemia like pernicious anaemia. It is also of the utmost importance that only simple iron preparations should be given; tablets or fluid preparations of ferrous sulphate, gluconate, carbonate, and fumarate are available and one of them will be found to suit any patient.[2] Preparations containing added vitamin-B complex must be avoided since they may contain folic acid. It is unwise to use compound haematinics, and preparations containing added calcium, magnesium, cobalt, and so on are unnecessary. Ascorbic acid can be given, but should be separate from the iron. On this treatment 9 out of 10 women patients with anaemia will respond and will not need further investigation. The one out of 10 who does not respond, together with all males and all women past the menopause, need further investigation. Fry has shown how, in favourable circumstances, much of this investigation can be carried out by the general practitioner himself utilizing the laboratory and radiological departments. Others may prefer to send the patient at once to a suitable hospital out-patient clinic for investigation, and in this case the fact that the degree of anaemia is already known should be a help to the consultant and his staff in determining the urgency of the case.

FEELING PAIN

A recent symposium on the assessment of pain in man and animals—held at the Middlesex Hospital under the chairmanship of Sir Russell Brain and organized by the Universities Federation for Animal Welfare—provided an opportunity for neurologists, neurosurgeons, psychiatrists, anaesthetists, and research workers in various fields to exchange views on the mechanisms, nature, and treatment of pain. The causation of pain is related to somatic sensation in general, but pain must be regarded as a specific sensation in its own right rather than the consequence of an intensification of stimuli normally giving rise to other somatic sensations. As evidence of this there are those rare cases[1 2] in which pain sensation is congenitally absent while the perception of other types of sensation is preserved. C. A. Keele and J. D. Hardy, speaking at the symposium, both showed that under carefully controlled conditions there existed an objective threshold above which pain was constantly evoked; below this level there were varying degrees of discomfort for which the term "metaesthesia" had been suggested.

So far as the peripheral nervous system is concerned there is still controversy between those who believe in specific fibres for each type of sensation and those who maintain that the pattern of impulses determines the kind of sensation which is felt. The original theory of specific nerve energies, though now considerably modified, still has distinguished proponents, while G. Weddell and his colleagues[3] at Oxford have provided indisputable evidence that, for example, all types of somatic sensation can be felt in the human cornea, in which only bare nerve endings are found. There seems no reason why both these theories should not be partly correct: certainly if information were not modified between the periphery and the cortex there would be no need for intermediate synapses. At the level of the first synapse, in the posterior horn of the spinal cord, P. D. Wall[4] has recently described "common carrier" cells which are "fired" by several different kinds of peripheral stimuli.

Within the central nervous system information is further modified at synapses as it ascends towards the cortex. Recent work tends to distinguish between two systems, with separate anatomy and functions. The lemniscal system, including the dorsal columns of the spinal cord, the medial lemniscus, and the spinothalamic fibres (spinal lemniscus), relay through the specific ventroposterior nucleus of the thalamus to the postcentral gyrus. This system responds to tactile stimuli, such as hair movement, applied to discrete areas of skin, and to movements of individual joints (kinaesthesia). Spatial discrimination within this system is heightened by the Sherringtonian phenomena of inhibition and occlusion.[5] In the other system, the extralemniscal, fibres run through and relay in the central reticular core of the brain stem.[6] Unlike lemniscal fibres they show very little spatial organization and are finally distributed to both cerebral hemispheres by the so-called diffuse thalamocortical projection. They converge upon and relay in certain of the intralaminar nuclei of the thalamus, and possibly also in other regions of the diencephalon, and are activated by such stimuli as pinprick and sharp

[1] Westlake, E. K., *Brit. med. J.*, 1952, **1**, 144.
[2] Ogden, T. E., Robert, Framoise, and Carmichael, E. A., *J. Neurol. Neurosurg. Psychiat.*, 1959, **22**, 267
[3] Lele, P. P., and Weddell, G., *Brain*, 1956, **79**, 119.
[4] Wall, P. D., *J. Neurophysiol.*, 1960, **23**, 197.
[5] Poggio, G. F., and Mountcastle, V. B., *Bull. Johns Hopk. Hosp.*, 1960, **106** 266.
[6] Bowsher, D., *Brain*, 1957, **80**, 606.
[7] Spiller, W. G., and Martin, E., *J. Amer. med. Ass.*, 1912, **58**, 1489.
[8] Ervin, F. R., and Mark, V. H., *Fed. Proc.*, 1961, **20** (Part I), 345.
[9] Head, H., and Holmes, G., *Brain*, 1911, **34**, 102.
[10] Macht, M. B., and Kuhn, R. A., *Arch. Neurol. Psychiat.* (*Chicago*), 1948, **59**, 754.

tapping. At the recent symposium D. Bowsher and D. Albe-Fessard stressed the virtual independence of the two systems, between which very little interaction can be detected below the level of the cerebral cortex.

In the spinal cord the extralemniscal fibres (together with the relatively unimportant lemniscal fibres of the spinothalamic tract) can be sectioned by anterolateral cordotomy, which has now been in use for fifty years as an effective operation for relieving pain.[7] Surgical attempts to destroy extralemniscal fibres selectively at higher levels have not hitherto been very successful owing to their deep and diffuse arrangement in the brain stem, though recently F. R. Ervin and V. H. Mark[8] have reported encouraging results in the relief of pain from stereotaxic destruction of the intralaminar nuclei of the thalamus without interference with other somatic sensation.

A careful distinction should be made between the conscious feeling of pain and motor reactions to a painful stimulus. Loss of the affective reaction to pain after bilateral prefrontal lobotomy shows that the integrity of the cerebral cortex is necessary for the full appreciation of pain: it does not "come to consciousness in the thalamus" as claimed in 1911 by H. Head and G. Holmes.[9] But owing to the profuse, though indirect, connexions of the extralemniscal pathways with subcortical motor centres, it is possible for violent motor reactions to painful stimuli to occur in the absence of any conscious sensation of pain. In contrast with this, discriminative tactile sensations, conducted over lemniscal pathways, do not give rise to motor reactions in the absence of the cortex.[10] This point should be particularly borne in mind when dealing with experimental animals. For example, the decorticate cat reacts with the same ululating alacrity to a hot tin roof as does the intact animal, although it does not "feel" pain, in the sense of conscious suffering. A proper concern for the welfare of laboratory animals should not lead to a blurring of the difference between conscious sensation of pain and the reaction to a painful stimulus; in appropriate conditions either can occur in the absence of the other.

The clinician is perennially faced with the problem of pain in the individual patient. He commonly sees great differences in the reactions to it, and they vary with the cultural and environmental background as well as with the circumstances in which pain is inflicted. H. K. Beecher explained at the symposium how the well-known difference in the degree of pain experienced by those wounded in battle or injured in civilian life could be quantitatively assessed by need for morphine. The conditions of the laboratory are very different from those of the surgery and the hospital ward, of the street accident and the battlefield. The stimulus is an objective phenomenon, tissue damage; pain, on the other hand, is a subjective sensation. Between the two lies a world of nervous impulses moving along pathways as yet incompletely known, subject to modification not only by other physical factors present at the time of the stimulus but also by psychological factors which are themselves highly variable, even within a single individual at different times and in different circumstances. How these factors modify the conscious sensation of pain is incompletely understood. But the clinician may take comfort from the fact that the problem of pain is now being more thoroughly studied in all its aspects than at any previous time, and we may look forward with confidence to further elucidation of its mysteries.

RECENT RESEARCH ON COALWORKER'S PNEUMOCONIOSIS

Three recent publications on the subject of coalworker's pneumoconiosis, two from the National Coal Board[1 2] and one from the Medical Research Council's Pneumoconiosis Research Unit and Welsh National School of Medicine,[3] give an opportunity of assessing the present state of research, particularly in the field of simple pneumoconiosis. The report by D. Hicks and his colleagues[1] is an impressive volume summarizing the analysis of 30,000 chest radiographs and industrial histories of coal-miners from twenty-six pits selected for the National Coal Board's Pneumoconiosis Field Research. The field work has been well organized and carefully carried out, the results skilfully analysed and beautifully presented. The material represents the baseline of an investigation into the aetiology of simple pneumoconiosis. The authors' findings are drawn from a retrospective study of present *x*-ray category and past industrial history, and possibly the report attaches too much importance to the relationship between the time taken for 20% or 50% of the miners at the various pits to develop a given category of pneumoconiosis and the type of coal mined in the pit. A better alternative might have been to postpone publication until the next round of *x*-ray surveys enabled the Coal Board to test the hypothesis by a prospective study, in which the changes in *x*-ray category can be related to the concentration of dust to which the miners have been exposed and to its chemical characteristics. The snags introduced by retrospective investigation in this sort of work are considerable. It is on the whole probable that in the past pits with one type of coal have been dustier

[1] Hicks, D., Fay, J. W. J., Ashford, J. R., and Rae, S., *The Relation Between Pneumoconiosis and Environmental Conditions*. National Coal Board, Pneumoconiosis Field Research, London, 1961.
[2] Rogan, J. M., *et al.*, *Brit. med. J.*, 1961, **1**, 1337.
[3] Cochrane, A. L., and Higgins, I. T. T., *Brit. J. prev. soc. Med.*, **15**, 1.

than those with another, and this alone might explain the results. In addition it appears that the method of analysis assumes that there have been no changes in concentration of dust in the past, so the hypothesis that dust concentration alone is the most important factor has hardly been investigated. The aetiology of simple pneumoconiosis remains puzzling. Most people will continue to believe, until more conclusive evidence is produced, that dust concentration is the most important factor, but there is clearly room for others, possibly related to the type of coal. Even so the Coal Board is to be congratulated on having established such a firm baseline. Most of the answers can be expected from the next round of their *x*-ray surveys.

In one of the other two studies J. M. Rogan and his colleagues[2] use the miners from 8 of these 26 pits to investigate the relationship between *x*-ray category of simple pneumoconiosis, pulmonary ventilatory capacity, and respiratory symptoms. In the other A. L. Cochrane and his colleagues[3] deal with the same problem using random samples of complete mining populations. The latter technique enables ex-miners to be included, but suffers numerically in comparison with the other. The results in the latter paper suggest, rather surprisingly, that there is little or no ventilatory disability associated with simple pneumoconiosis and even more surprisingly that there appears to be an important difference in ventilatory capacity between miners and ex-miners of the same age and of the same *x*-ray category in Derbyshire and the Rhondda. Rogan and his colleagues on the contrary find a slight but distinct loss of ventilatory capacity with increasing category of pneumoconiosis, the loss being greatest in category 3. One sentence in their paper suggests that regional differences in ventilatory capacity are also found, but as all the data from the eight pits are combined they are presumably unimportant. No other country in the world could produce one, let alone two, such examples of large-scale accurate epidemiological work in this field, and it is perhaps unfair to be critical, but it seems unfortunate that the two teams of workers use different age groups, express their physiological findings in different units, and do not discuss each others' results. Until agreement is reached between these two groups on whether simple pneumoconiosis causes disability or not the outsider must reserve judgment, but it seems probable that the disability, if present, is very slight. The fog is slowly lifting from the problem of pneumoconiosis, and this seems to be due more to the high level reached by epidemiological methodology in Great Britain than to any other single factor.

HYPERURICAEMIA

The advent of new and effective drugs such as probenecid, sulphinpyrazole, and zoxazolamine which increase renal excretion of uric acid has directed more attention to some other aspects of hyperuricaemia. In practice this term signifies a uric-acid level in the plasma of 6 mg. or more per 100 ml. in men and 5.5 mg. or more per 100 ml. in women. The relationship of uric acid to renal function in particular is of some interest and may be of considerable importance. It seems clear that hyperuricaemia may of itself impair the kidneys either because of deposits of excess urate in them[1] such as may arise in blood dyscrasias or through some other mechanism. While approximately one-third or more of patients with primary gout produce excessive urate,[2] in other cases the renal clearance is too low[3] and is probably the cause of the hyperuricaemia. In secondary gout excessive urate may be produced owing to disorders of blood and reticulo-endothelial systems,[4] but there may also be a reduced clearance of urate owing to the administration of diuretics[5] or pyrazinamide.[6]

The relationship of hyperuricaemia to pregnancy has recently been investigated by B. L. J. Treadwell and A. St. J. Dixon.[7] It seems that while in normal men there is no variation of the level of serum uric acid with age, in women the level is usually at least 1 mg. per 100 ml. lower and there is an increase with age, especially after the menopause.[8 9] Only 5–10% of sufferers from gout are women[10] and most of these are past the menopause. The conception rate of women with gout is low[11] and most of the pregnancies end before term. During pregnancy, which is therefore rare,[12] symptoms of chronic gout are usually much relieved and acute episodes suppressed, but acute attacks usually develop in the puerperium or after abortion. This has led to the suggestion that oestrogens have an inhibitory effect on gout.[13]

Several workers have shown that toxaemia of pregnancy is associated with hyperuricaemia and renal impairment.[14 15] In most cases retention of urate has been unrelated to reduction in glomerular filtration and has been attributed to increased reabsorption by the renal tubules.[16] The possibility of decreased filtrability of the urate has been considered but not proved. A. B. Gutman and colleagues[17] have shown that tubular secretion of urates can take place, and impairment of this mechanism would appear to be a possible explanation of the hyperuricaemia. In Treadwell and Dixon's series 88 cases of pre-eclampsia were studied, and it was found that the number with hyperuricaemia rose from two at five weeks before delivery to fourteen in the week preceding delivery and a maximum incidence of 17 (19%) in the first week post-partum, and fell to 8 in the following week. However, even four months later two patients still had a serum uric acid of over 6 mg. per 100 ml. In the average case the serum uric acid rose

[1] Greenbaum, D., Ross, J. H., and Steinberg, V. L., *Brit. med. J.*, 1961, **1**, 1502.
[2] Gutman, A. B., and Yü, T. F., *Amer. J. Med.*, 1957, **23**, 600.
[3] Nugent, C. A., and Tyler, F. H., *J. clin. Invest.*, 1959, **38**, 1890.
[4] Talbott, J. H., *Medicine (Baltimore)*, 1959, **38**, 173.
[5] Freeman, R. B., and Duncan, G. G., *Metabolism*, 1960, **9**, 1107.
[6] Yü, T. F., Berger, L., Stone, D. J., Wolf, J., and Gutman, A. B., *Proc. Soc. exp. Biol. Med.*, 1957, **96**, 264.
[7] Treadwell, B. L. J., and Dixon, A. St. J., *Ann. rheum. Dis.*, 1961, **20**, 186.
[8] Hewitt, V., ibid., 1960, **19**, 380.
[9] Praetorius, E., *J. Geront.*, 1951, **6**, 135.
[10] Bauer, W., *New Engl. J. Med.*, 1943. **229**, 583.
[11] Talbott, J. H., *Gout*, 2nd edition, 1957, New York.
[12] Friedman, E. A., and Little, W. A., *Amer. J. Obstet. Gynec.*, 1958, **76**, 913.
[13] Weingold, A. B., *Obstet. & Gynec. (N.Y.)*, 1960, **16**, 309.
[14] Chesley, L. C., *Amer. J. Obstet. Gynec.*, 1950. **59**, 960.
[15] Cadden, J. F., and Stander, H. J., ibid., 1939, **37**, 37.
[16] Seitchik, J., Szutka, A., and Alper, C., ibid., 1958, **76**, 1151.
[17] Gutman, A. B., Yü, T. F., and Berger, L., *J. clin. Invest.*, 1959, **38**, 1778.
[18] Pollak, V. E., and Nettles, J. B., *Medicine (Baltimore)*, 1960, **39**, 469.

to a maximum just before delivery and then fell gradually over the next few weeks. The total incidence of hyperuricaemia at all stages was 26% (23 cases). V. E. Pollak and J. B. Nettles[18] had previously shown that there is a close correlation between hyperuricaemia and glomerular changes seen on renal biopsy in toxaemia of pregnancy, and Treadwell and Dixon conclude that their work indicates that renal cellular damage due to toxaemia of pregnancy persists for a variable period into the puerperium. An interesting feature of this type of renal impairment is that the blood urea was not raised in any of the 23 cases, so it would seem that estimations of the serum uric acid provide the most sensitive indication of renal impairment in pre-eclampsia. Whatever its aetiology, the hyperuricaemia is transient and symptomless and does not provide an indication for uricosuric therapy.

THE QUICK AND THE DEAD

Assessment of the viability of damaged tissue is of great clinical importance in the care of the injured. Primary excision and grafting of deep burns depend on sure knowledge of the extent of full-thickness skin destruction. Compound fractures with extensively damaged skin call for a decision whether to suture and hope or to ensure skin cover by using a flap. Similar problems are presented by partially flayed and degloved limbs, by crushed or electrically damaged muscle, and by bruised gut.

Simplicity of procedure is often the secret of success in surgery, but the surgeon must resist oversimplifying the problem. The usually accepted criteria of tissue viability are the presence of a blood supply and the ability of nerves to feel and muscles to contract. But Nature is seldom so accommodating as to deny herself exceptions. The presence of a blood supply is not always a sign of viability. Tissue burned to the intensity characterized by capillary stasis may have a circulation for hours, but it is doomed; and, again, the death of skin flaps is due most commonly to impairment not of blood supply but of venous drainage. Conversely, the *apparent* absence of blood supply is no index of the death of an organ like the skin, for skin has depth, and apparent and real necrosis of the surface may mask living epithelial elements half a millimetre below the surface. In the diagnosis of partial and full-thickness skin destruction sensitivity can be a valuable sign: the appreciation of pinprick in burned skin means partial damage only, and healing will occur in less than 3 to 4 weeks. Analgesia of the skin can be due to many factors and is a less valuable prognostic sign.[1 2] Doubt about what is living and what is dead is frequent, and it will make the surgeon play for safety. Sometimes safety will dictate a conservative course—burned skin that might be viable will be preserved to lessen scarring—sometimes, as with doubtfully viable bowel, it will demand radical excision.

In the last two decades surgeons have turned repeatedly to dyes for help in this problem. Fluorescein,[3] Kiton fast green,[4] and "disulphine" blue[5] have been used as intravenous injections, and a modified van Gieson's stain has been applied to the surface of burns to show up dermal necrosis.[6] The intravenous dyes display the state of the circulation, but in burns this can be assessed more simply by pressing on the skin with a sterile forceps. Moreover both intravenous and surface dyes only provide pre-operative information as deep as the eye can see, whereas the critical layer in burns is the deepest plane of epithelial elements. It would be hard indeed to better Nature's "dye." This is not a solution in the plasma but the red cell itself. Burned tissue which is doomed to stasis and death becomes vascular *and red* during the first 24 hours, and it remains red for about 3 to 4 days till the corpuscles lyse, indicating the boundary of necrosis. This is an excellent guide at operation. However, the doubtful value of injected dyes in burns does not exclude their possible usefulness in other fields, such as the appraisal of crushed muscle or damaged bone, and further investigation may yet give these dyes a bigger place among our clinical tools.

GALLOP RHYTHMS

Recordings of the heart sounds in healthy people reveal two sounds which the ear cannot usually detect as well as the normal first and second sounds. These "sounds" become audible in certain circumstances and then the listener hears a "triple" or "gallop" cadence in the heart rhythm.

The first of the "sounds" is the third heart sound, which is thought to occur in the following manner. Blood is returned to the heart throughout systole and diastole; during systole it cannot pass into the ventricles because the mitral and tricuspid valves are closed and it becomes dammed up in the atria. In diastole the ventricle relaxes, these valves open, blood rushes into the ventricles from the atria, and this stretches the ventricular walls. This sudden stretching produces a noise rather in the way the wind will produce a noise as it fills an empty sail. As diastole progresses the ventricles continue to fill from the atria through the atrio-ventricular valves, which are wide open. Towards the end of diastole the atria contract, thus "supercharging" the ventricles by squeezing into them some of the blood which remains in the atria. This squeeze from the atria is sudden and stretches the already partially stretched ventricular wall. Once again a small and normally inaudible "sound" is produced. These two sounds may be accentuated in various ways and they then reach levels at which they can be heard with the stethoscope. When the third heart sound is audible, as it frequently is in normal children, it produces the third-

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heart-sound gallop. When the atrial sound is audible it produces the atrial gallop.

If a normal person has tachycardia diastole is shortened and the atrial "sound" follows so soon after the third heart "sound" that the ear gets the impression that they are synchronous. When this occurs the addition of two previously inaudible elements to each other may bring the volume of sound up to the level which the ear can detect. This is the so-called "summation" gallop, and unlike the other two it can occur in healthy adults.

These three types of gallop—the atrial, third-heart-sound, and summation—are all caused by ventricular filling and they are the only ones we recognize to-day. The simple nomenclature based on the physiology of the heart has helped to clear up some of the previous confusion, which was caused in part by the curious nomenclature adopted by earlier authors.

Gallop rhythms may be produced either in the left side of the heart or in the right, as a result of disease which increases the intensity of the atrial or third heart "sounds," and sometimes both of these may be heard together, producing a four-beat cadence. If a gallop is produced in the left ventricle it is usually heard best at the apex during expiration; if in the right ventricle, it is usually heard to the left of the sternum at its lower end during inspiration. An atrial gallop usually indicates that the related ventricle is working under stress. Thus a left atrial gallop rhythm may be heard in essential hypertension or in cardiac infarction. A right atrial gallop may be heard in pulmonary stenosis or in pulmonary hypertension. A third-heart-sound gallop may be heard in heart failure, in mitral incompetence, or in constrictive pericarditis, and it implies that the pressure in one or other of the atria is raised and that rapid filling of the ventricle occurs through a widely open or dilated atrio-ventricular valve.

FACIAL PALSY

The difficulties of assessing the effects of treatment in conditions which have a high rate of spontaneous recovery are considerable. It is usually assumed that if treatment is to be effective it must be carried out in the first few days after onset. On the other hand, spontaneous recovery rates are highest during this time and it seems reasonable to wait to see if the individual patient will recover on his own. In a most useful account of the natural history of Bell's palsy W. B. Matthews[1] has described a series of cases in which those examined in the first two days showed a recovery rate of 85% provided that the patients suffering from herpes were excluded. The group of patients examined up to six days after onset showed 68% recovery, again with the exclusion of herpetic cases. Such figures strengthen the view that it is worth waiting for spontaneous recovery.

Accurate prognosis would be easier if electrodiagnostic tests were reliable in predicting incomplete recovery when performed within a few days of the onset of paralysis. Unfortunately this does not appear to be the case. On electromyographic examination fibrillation is often absent, and its failure to appear cannot be regarded as a sign of an incomplete lesion. Progressive disappearance of muscle action potentials under voluntary control and in response to electrical stimulation of branches of the facial nerve probably indicates that recovery will be long delayed or incomplete. R. W. Gilliatt and J. C. Taylor[2] accept that examination as long as two weeks after the onset of Bell's palsy may be necessary before one can be sure that the distal part of the nerve is not going to degenerate. They also observed that electromyographic examination may reveal surviving units in response to nerve stimulation at a time when no twitch is visible in the muscles. Matthews's figures indicate that it is useful when considering prognosis to know whether the lesion is complete or partial at 14 days after onset. Out of 72 patients in whom the lesions were partial at 14 days, including lesions which had originally been complete, 61 (85%) recovered, the rates of recovery being much lower for cases showing complete palsy at this time. Electrical examination such as that used by Gilliatt and Taylor may thus be helpful in showing failure of conduction or preservation of intact units.

However, the decision to carry out active treatment such as surgical decompression of the facial nerve or sympathetic block[3] appears still to be based on clinical impressions and the circumstances of the individual patient. This rather unsatisfactory situation will exist until effective treatment which is without hazard or unpleasant side-effects can be given to all patients in the early stage of paralysis. Alternatively, tests designed to predict the course of recovery may be devised. If they are to be useful they must give the answer within the time during which therapy will be effective.

Matthews's experience with surgical treatment in five patients who showed no improvement after twelve weeks was not encouraging. His plea for careful matching of controls in any trial of therapy is backed by his demonstration of variations in recovery between clinical groups, according to duration since onset, age, degree of paralysis, and presence of herpes. All of these affect the outlook. Hence the basis of comparison between treated and untreated groups in a trial may be vitiated by failure to recognize these effects.

G. A. Dalton[4] also emphasized the difficulty of evaluating the effects of surgical decompression in his cases. It is obvious that thorough investigation of the prognostic value of electrodiagnostic tests and of the effects of both medical and surgical treatment is necessary. In view of this it is not possible to lay down any fixed scheme for the management of these patients at the present time. Supportive measures such as galvanism and slings may possibly be useful. If cosmetic surgery is likely to be needed it is helpful to maintain the mobility of the facial tissues by massage.

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ADMISSION OF ELDERLY PEOPLE TO HOSPITAL

RELATIVE IMPORTANCE OF MEDICAL AND SOCIAL FACTORS

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As a result of the publicity given to the social aspects of old age many people assume that the problems created by the aged in our population are social rather than medical in origin. In this paper we report a survey which was carried out to determine the relative importance of the medical and social factors which led general practitioners to refer a group of elderly people for admission to hospital.

Material and Methods

During the 12-month period from January 1 to December 31, 1957, we visited at home as many of the people as possible who were referred to us for admission by their own doctor. We excluded those classed by their doctor as acutely ill. Such cases were generally admitted within 48 hours without prior visiting. We visited 558 patients, all of whom had been referred by their doctor—the majority for admission, a few (approximately 20%) for a medical opinion. In most cases information about the patient was given by the G.P. to a central bed bureau. This information was typed on to a punched card, specially designed for this survey. About 50 patients were seen by one of us (W. H. L.) alone; the remainder were visited by both of us at the same time. The patients were visited once at home; the medical and social information gathered on this visit was in many cases amplified in subsequent interviews in the out-patient department or hospital wards. The G.P. was present at about 20% of these visits.

Results

When we considered the G.P.s' reasons for referring patients for admission to the geriatric unit, we found that these could be grouped as follows:

1. *Medical Reasons.*—(*a*) Those cases where the G.P. felt uncertain of the diagnosis and sought a medical opinion. (*b*) Those cases where the G.P. was confident of the diagnosis but experienced difficulty in carrying out the appropriate treatment at home.

2. *Social Reasons.*—In this group the medical condition of the patient was thought to be relatively unimportant by the G.P. (*a*) He thought the patients in this subgroup were in need of nursing care and attention, which he felt could not be maintained at home. (*b*) He felt that the nursing care and attention given at home was adequate. He referred these cases to hospital because of the pressure exerted on him by those caring for the patient.

Table I shows the age-and-sex distribution of the sample. Table II shows the action taken in the cases of those visited at home: 59% were subsequently admitted to the geriatric unit. They formed 29% of the total number (1,139) of people admitted to the unit in the 12-month period. The remaining 71% were admitted as emergencies or from the out-patient department.

Table III shows the distribution of the "medical" and "social" cases according to sex and to the action taken: 66% of the social group and 40% of the medical group were admitted to the unit.

TABLE I.—*Age-and-Sex Distribution*

Age:	<50	50–	55–	60–	65–	70–	75–	80–	85+	Not Known	Total
Males	1	3	6	18	23	59	43	27	14	4	198
Females	9	6	10	31	31	91	73	74	28	7	360
Total	10	9	16	49	54	150	116	101	42	11	558

TABLE II

	Action Taken				
	Out-patient	In-patient	Welfare	General Practitioner	Other Hospital Departments
Males ..	42	107	3	39	7
Females ..	50	220	8	75	7
Total ..	92 16·5%	327 58·5%	11 2%	114 20·5%	14 2·5%

TABLE III

	Action Taken					Total
	Out-patient	In-patient	Welfare	General Practitioner	Other Hospital Departments	
Medical Group						
Males ..	19	22	—	18	2	61
Females ..	24	38	—	26	3	91
Total ..	43 28·3%	60 39·5%	— —	44 29%	5 3·2%	152 100%
Social Group						
Males ..	23	85	3	21	5	137
Females ..	26	182	8	49	4	269
Total ..	49 12%	267 65·7%	11 2·9%	70 17·2%	9 2·2%	406 100%

We have undertaken a comparison of these two groups on a number of different counts:

1. *Age.*

2. *Sex.*

3. *Marital Status* (Table IV).—Each group closely followed the whole sample.

4. *Housing* (Table V).—There was no significant difference between the two groups.

5. *Household Composition* (Table VI).—The following groups were differentiated: (*a*) those living with spouse; (*b*) those living with relatives; (*c*) those living

TABLE IV.—*Marital Status*

	Married		Single		Widowed		Separated	
	No.	%	No.	%	No.	%	No.	%
Males	80	40·4	11	5·6	105	53·0	2	1·0
Females	76	21·2	49	13·7	231	64·1	4	1·0

TABLE V.—*Type of Housing*

	Medical Group		Social Group	
	No.	%	No.	%
Old person's bungalow ..	3	2	23	5·6
Back-to-back house ..	4	2·7	13	3·2
Terrace house	109	71·8	269	66·3
Council ,, ...	10	6·6	43	10·5
Modern ,, ...	8	5·3	29	7·2
Hostel	6	3·8	12	3·0
Other*	12	7·8	17	4·2

* Farmhouses, public houses, shops, etc.

in lodgings or with friends, and (*d*) those living alone. It will be seen from Table VI that 17% of the medical group lived alone, whereas 32.7% of the social group lived alone. In Table VII the medical and social groups have each been divided into three according to the household composition. Medical and social group A are those people living with relatives or spouse; group B, those living in lodgings or with friends; and group C, those living alone. The action taken in each group is shown. The figures in the medical group are too small to judge any difference between the subgroups. The finding that 63% of social group A and 71% of social group C were admitted to hospital suggests that the fact of living alone was not of supreme importance in causing their admission to hospital.

TABLE VI.—*Household Composition*

	Medical Group		Social Group		Total	
	No.	%	No.	%	No.	%
Living with spouse	47	31	109	26·9	156	27·9
,, ,, relatives ..	67	44	138	33·9	205	36·8
Living in lodgings or with friends	12	8	26	6·5	38	6·9
Living alone ..	26	17	133	32·7	159	28·4

TABLE VII

	Out-patient		In-patient		Welfare		G.P.		Other Hospital		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
Medical Group											
A ..	32	28·1	41	36	—	—	38	33	3	2·6	114
B ..	3	25	6	50	—	—	2	16·7	1	8·3	12
C ..	8	30·7	13	50	—	—	4	15·4	1	3·9	26
Social Group											
A ..	25	10·5	155	62·6	2	0·8	57	23	8	3·1	247
B ..	4	15·4	17	65·4	2	7·6	3	11·6	—	—	26
C ..	20	15	95	71·4	7	5·3	10	7·5	1	0·8	133

6. *Duration of Illness.*—An attempt was made in every case to assess the duration of illness. Although no accuracy was possible on this score, the majority of medical cases presented with an illness measurable in days or weeks, while most of the social cases presented with an illness measurable in months or years.

7. *Medical Condition.*—A clinical diagnosis was made in every case after a history and physical examination. The distribution of diseases diagnosed according to the *International Classification of Diseases* is shown in Table VIII. This illustrates a wide distribution of diseases with a maximum incidence of disease in groups II, VI, VII, and VIII. We feel that the high incidence in the social group of diseases in group VI is significant.

Discussion

Our results suggest that the differences between the medical and social groups as classified by the general practitioner were:

1. *In the Duration of Illness.*—It is possible to make the generalization that the patients in the social group had been ill for so long that they and everyone attending them had almost forgotten that they had ever been well, whereas the medical group still remembered what it was like to be well.

2. *Type of Illness Suffered by Patient.*—Of the social group 62% were judged to suffer from diseases of the cerebrovascular system.

We were much interested in the genesis of the social cases. We felt that they had become socially crippled by disease; many had progressed to the point of personal demoralization and were partially or completely rejected by their relatives.

We were in no doubt that the most important factor in producing the tensions which we found in the social group was the feeling, often shared by the patient and those caring for him, that "nothing more could be done." The patient's awareness of this attitude had in the course of time resulted in his demoralization and regression, which in turn did nothing to slow the process of rejection. We found, however, that many of the social group were suffering from conditions which could be alleviated sufficiently to allow them to return to some sort of life outside hospital. The problem of reorientating patients and their relatives in such circumstances is often long and difficult, and we are preparing a further paper dealing with this aspect of the problem. It is sufficient to say that of the 267 cases in the social group admitted to hospital 120 (44%) were satisfactorily resettled at home.

The position of the general practitioner, who is primarily responsible for the care and treatment of these patients, is unenviable. At the present time, despite the fact that as much as 25% of the general practitioner's time is taken by the elderly sick, little or no instruction in this field is given to the medical student. One result of this is to be seen in the confusion regarding the ageing process. Although the normal process of ageing remains to be defined, many people still believe that age alone can be responsible for all sorts of symptoms and signs. One disease that appears to be commonly confused with ageing is hypothyroidism (Lloyd and Goldberg, 1961); as more work in this field is done, further similar diseases will probably emerge. If to all this is added the fact that in most areas it is difficult to get an elderly person into hospital, it is not hard to understand how the patients in the social group came to be so labelled.

We feel that the social group referred to us for admission are analogous to the institutionalized "inheritance," which almost all newly appointed geriatricians find occupying their hospital beds. The social group largely represent the surplus of sick people, many meriting further hospital investigation and treatment, who wait too long for investigation and treatment simply because there are insufficient hospital facilities for them at present.

There is a tendency to overlook the fact that hospitals derive their patients primarily from the general practitioner. In assessing the needs for hospital beds it is important to bear in mind this part played by the

TABLE VIII

	I	II	III	IV	V	VI	VII	VIII	IX	X	XII	XIII	XVI	XVII
Medical Group														
No.	3	16	6	4	4	38	37	16	8	8	2	8	—	2
%	1·8	10·6	39	27	27	25	24·3	10·6	5·2	5·2	1·4	5·2	—	1·4
Social Group														
No.	4	42	14	5	5	179	79	50	5	5	3	13	—	2
%	1	10·4	3·5	1·2	1·2	44·2	19·4	12·3	1·2	1·2	0·7	3·2	—	0·5

general practitioner. In certain circumstances he tends to be a very variable factor. We feel that, in the field of the elderly sick at least, insufficient attention has been paid to the factors which may influence the demands made by general practitioners on their local hospital services. In any area lacking a comprehensive geriatric service many general practitioners will have become accustomed to the inability of their hospital service to help them with most of the problems they encounter with their elderly patients. In such an area it is likely that many patients falling into our social group never appear on a hospital waiting-list because the beds available are only sufficient to take those whose social circumstances have so deteriorated that it is impossible for them to exist outside hospital. Such cases usually exhibit irreversible physical and mental deterioration and tend to perpetuate the bed shortage.

A recent survey of all the Birmingham hospitals (McKeown *et al.*, 1961) has demonstrated the need of a very high proportion of elderly patients admitted to hospital for beds with full hospital facilities. It has been the experience of one of us (W. H. L.) in two different areas that the establishment of a comprehensive geriatric unit uncovers unexpectedly large numbers of elderly people who benefit from in-patient or out-patient general hospital investigation and treatment. This observation suggests that the need in any area for comprehensive geriatric beds will not be known until a comprehensive service exists and there is local knowledge amongst the general practitioners of its potentialities.

It is clear that much can be done for many of the social group; more can be done more quickly if they are dealt with early in their illness. We feel that many require a period in hospital.

During their stay in hospital most will initially need all the facilities of an " acute " medical bed for adequate medical assessment; many will then require a period of physical and mental rehabilitation. During this latter period an accurate assessment of their domestic and social circumstances must be made if they are to be satisfactorily resettled outside hospital. This implies a rather more constructive and perhaps wider sphere of action than is generally apportioned to the geriatric unit, but it is in general accordance with McKeown's (1958) concept of a balanced hospital community. In our experience it would seem that such a comprehensive geriatric service is a logical answer to the problem and that it is not more hospital beds that are required for this service but rather better use of existing beds. It follows from what has been said that in any area served by such a unit the number of social cases encountered will gradually decline with the passage of time.

Summary and Conclusions

During a 12-month period, and from an overall population of about 250,000, 1,370 elderly people were referred by their own doctor for admission to a geriatric unit. Of these, 558 were selected and visited in their home. The method of selection is defined. This sample was assessed from the social and medical points of view, details of which are given. An attempt has been made to define the relative importance of the medical and social factors which caused general practitioners to refer this group of their elderly patients for admission to a geriatric unit.

We have concluded that: (1) social problems in the elderly are usually secondary to demonstrable physical disease; (2) with proper hospital facilities, a high proportion of elderly people socially crippled by disease can be satisfactorily rehabilitated for life outside hospital; (3) lack of proper hospital facilities for the elderly often results in social crippling by disease; and (4) a comprehensive geriatric service is a logical solution to the problem of the elderly sick, and if properly applied would ultimately prevent the accumulation of many of the " social problems of old age."

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EXPERIMENTS WITH THE CURRICULUM

ASSOCIATION FOR THE STUDY OF MEDICAL EDUCATION

[FROM A SPECIAL CORRESPONDENT]

On December 7 the Association for the Study of Medical Education held a meeting at the Middlesex Hospital Medical School to discuss changes which individual medical schools have made in their curriculum. Sir ROBERT PLATT, P.R.C.P., chairman of the association, opened the meeting by commenting on the fact that four years had elapsed since the G.M.C. had set the medical schools free to arrange their own curriculum. Schools throughout the country had all been working on this and the discussion would be a preliminary exchange of views based on the changes introduced at Sheffield, Birmingham, and Glasgow.

Changes at Sheffield

Professor C. H. STUART-HARRIS described how thoughts on a new curriculum had begun in 1955, and in 1957 the G.M.C.'s recommendations had invoked flexibility in what had otherwise been a rigid course of instruction and appointments. They had found that there was a marked loss of interest among students in clinical appointments at the end of the fourth year owing to the proximity of the pathology examinations claiming their greater attention. The object at Sheffield was to preserve the students' interest in the three facets of teaching—clinical appointments, lectures, and examinations—without the presence of conflicting obligations. Thus in the fourth year Part I of the final M.B., Ch.B. examination was held in pathology, bacteriology, pharmacology, and clinical subjects. Thereafter all systematic lectures and demonstrations in these subjects ceased. Part II of the finals occurred in the fifth year in obstetrics and gynaecology, preventive medicine, public health, child health, and special subjects (dermatology, ophthalmology, oto-rhino-laryngology), leaving the sixth year free for the teaching of medicine and surgery. Part III in surgery, medicine (including psychiatry), and clinical science was the final, qualifying examination.

The course included two elective periods, in the fourth and fifth years. Time for this was obtained by shortening the length of some of the clinical appointments (e.g., obstetrics and gynaecology to three months), though medicine and surgery were maintained as six-month appointments. Integrated lectures, clinico-pathological

conferences, and biopsy meetings had been introduced, and the tutorial system was being tried out. There was also integration backwards into the preclinical years with clinical demonstrations with the object of enhancing the junior students' interest.

Dr. J. G. McCRIE discussed the entry into medicine and showed how, as more and more students obtained exemption from 1st M.B. by taking the "A" levels at school, the first-year entry fell but second-year entry rose. The 2nd M.B., Ch.B. course was still five terms, but was now more rational and integrated than before. Less time was spent in personal dissection, which was replaced by demonstrations. The elective period had proved of great interest. Projects covered many and diverse facets of medicine, such as surgery in Stockholm, surgery in the R.A.F., work with G.P.s, industrial medicine, work with prison medical officers, and even studying injuries with Wolverhampton football team. The tutorial system and tutors helped the students in planning their elective periods. The design of the new examinations in the fourth, fifth, and sixth years had helped in the progressive assessment of the students. The final Part III examination was judged by all examiners, and it was at this stage that honours and prizes were decided.

Professor G. M. WILSON dealt in more detail with the fourth-year curriculum and stressed how closely it was linked with the teaching in the hospital. The fourth-year examination was an integrated examination between the three subjects of pathology, bacteriology, and pharmacology. The examination consisted of two three-hour papers with questions cutting across all three subjects, an essay in pharmacology, tests in clinical methods, and a thirty-minute oral examination in front of all three examiners. Generally students passed or failed, but they might be referred in one subject. As failures sat the examination again in September, this inevitably interfered with the elective period.

Sir ROBERT PLATT opened the discussion by reiterating his opinion that the G.M.C. were really setting the schools free to arrange their own curriculum and that they would look favourably upon any logical course of instruction. He then commented upon examinations and queried their necessity.. Professor STUART-HARRIS thought that examinations remained a necessity until the staff–student ratio was substantially increased so that accurate assessment of individual students could be obtained. Mr. D. H. PATEY (Middlesex Hospital, London) said it was always easy to put new things into a curriculum, but how and what to leave out was more difficult. The mechanics of achieving this in a democratic community were formidable.

Apprentice Method at Birmingham

Professor A. L. D'ABREU (Birmingham) began by saying that at Birmingham the object of the new curriculum was to turn out university graduates in medicine. It would be an impertinence on their part even to think of turning out specialists in general practice or any other specialty. With this in mind they had attempted to restore the traditional British method of teaching—that is, the apprentice method—which was becoming lost owing to the infiltration of systematic lectures in pathology, pharmacology, etc., occupying so much of the students' time. In their new curriculum all systematic lectures, including—and here Professor d'Abreu took a deep breath—pathology, had been abandoned, and no lectures took place before 4.30 p.m. This left the students time to spend the whole day in the wards and clinics.

He discussed a more rigid standard of entry into medicine. The minimum requirements were three "A" levels with the candidate obtaining at least 50% in each subject. Encouragement was given to first-year applicants having good "A" levels in subjects other than those of the premedical course. He deplored the lamentable lack of knowledge of mathematics among medical students. In the premedical course botany and zoology had been replaced by a new course in biology, and a similar integration of chemistry and physics was being considered. The burden of memorizing topographical anatomy had been lessened in Birmingham by abolishing systematic lectures; by teaching anatomy to students in small groups; by reducing the amount of anatomy that students had to absorb; by reducing the time spent in the dissecting-rooms to around 300 hours (nine months); by concentrating topographical anatomy, along with micro-anatomy, radiological and surface anatomy, and embryology, into the first two terms of the preclinical course, and by having the examination in this subject before the student began his study of physiology and related subjects.

Yearly Examination at Glasgow

Professor C. M. FLEMING outlined the distribution of teaching hospitals in Glasgow and described the old curriculum. The new curriculum was spread over six years with an examination at the end of each year: 1st year premedical, 2nd year preclinical, 3rd year paraclinical and clinical, 4th year integrated studies, 5th year specialty classes and intensive studies, and 6th year intensive studies. Study of anatomy was reduced to three terms, and physiology was divided into physiology and biochemistry; there were thus three subjects for the preclinical examination. In the third and fourth years, after the examination, the course consisted of more physiology, pathology and bacteriology, materia medica, medicine, and surgery. This was the period of integrated studies with an examination at the end of the year. The fifth year was devoted to the specialties—for example, public health, psychological medicine, dermatology, ophthalmology. During the course there were clinico-pathological conferences, symposia, panel discussions, and seminars. The final year was a period of intensive study and revision, which took place at two main teaching hospitals, the Western and the Royal Infirmaries. This reduced the students' travelling time and kept them together during this critical year. During the intensive year the students had no outside obligation other than to the department to which they were attached.

Biology at the Middlesex Hospital

Any medical student who starts his career by attending Professor D. R. NEWTH'S course in biology at the Middlesex Hospital is very fortunate, for here there is an exciting and imaginative introduction to medicine. The course is full of such subjects as genetics, statistics, evolution, embryology, growth, ageing, immunology, animal behaviour, regeneration, and wound healing. Professor Newth pointed out that the biologist could not exist in isolation; he was part of the unit and needed other biologists around him in order to flourish. In a teaching hospital the biologist should influence the curriculum in the premedical, preclinical, and clinical years. Already at the Middlesex Hospital his department lectured to the 2nd M.B. students on such subjects as nuclear cytoplasmic interactions, animal behaviour, human somatotypes, statistics, autoradiographic techniques, ageing, transplantation of tissues, the genetical effect of ionizing radiation, the biology of fertilization, and infertility. In the clinical years they gave lectures on genetics, the patient in a population, and the genetical basis of tissue transplantation. The biologist in a medical school had a far greater intellectual contact in width on many subjects than his clinical colleagues, but immediately any of these became clinical entities then the clinicians at once obtained a far greater knowledge in depth of the subject.

Comments and Conclusions

Throughout the discussions which followed the principal speakers, the entry into medicine was criticized. The opinion was expressed that perhaps our students entered medicine too early and that physics, chemistry, and mathematics at "A" level at school were a better preparation than the botany and zoology taught there. The behaviour of our students and their attitude to work and games were contrasted with those of their more serious, more adult, and more hard-working counterparts in the U.S.A. who had entered medicine after a four-year liberal arts course.

The anatomy curriculum in the provincial universities, if not in London, appeared to be undergoing a change; the course is to be reduced to three terms and the "tyranny of the dissection-room" seems to be over. The preclinical course now consists of four subjects: anatomy, physiology, biochemistry, and pharmacology. There was also universal realization that for some unexplained reason students lose interest in medicine in their fourth year when the course should be at its most exciting phase. Attempts are being made to recapture their interest by avoiding conflicts of loyalties, reducing the congestion of the curriculum and avoiding tedious repetition, by introducing new and more exciting methods of teaching such as clinicopathological conferences, seminars, integrated lectures, symposia, and panel discussions, and by closer individual supervision and appreciation of their difficulties and problems through the tutorial system.

GETTING THEM BACK TO WORK

REHABILITATION AT PERIVALE

Sometimes the disorder from which a patient has recovered makes it physically impossible for him to return to his old job; sometimes the long spell away from work results in complete loss of confidence in his ability to work. In a few cases the patient is so reconciled to his idleness that work holds no attraction and he is content to spend the rest of his life on the dole.

In these cases, when medical rehabilitation can do no more, rehabilitation at an industrial rehabilitation unit (I.R.U.) is a logical step, since its aim is to help mentally or physically disabled men and women back to their full working capacity and to give them professional guidance about the kind of work likely to be most suitable for them.

The I.R.U. at Perivale

One of the most recent I.R.U.s is at Perivale in Middlesex; it lies in a modern factory area and is attached to the existing Government Training Centre. Apart from the administrative offices there are industrial workshops, an education section, a remedial gymnasium, and a meeting hall. The unit can take about 100 people at a time, and it draws them from 22 employment exchanges in the north-west of London. Recommendations for a course of industrial rehabilitation are most often made by hospitals—there are 50 within a seven-mile radius of Perivale—and general practitioners, through the Disablement Resettlement Officer (D.R.O.) at the nearest employment exchange. Trainees receive allowances while they are at the unit, and daily travelling expenses are paid.

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Perivale's Programme

Trainees normally stay at the unit for about eight weeks, and at the most for 12 weeks. During the first week they are seen by the unit's team of experts. The doctor assesses the applicant's condition and the effect of his particular disabilities on the work that he can do, and recommends whatever remedial exercises may be helpful. He is interviewed by the social worker and the unit's own D.R.O., and tested for his abilities and aptitudes by the vocational officer, an industrial psychologist who tries to help him take a realistic view of the kind of work he may later do. During this exploratory week the trainee works in the Intake Section Workshop. Here his skill, his ability to absorb instructions and mix with other people, and his reaction to supervision and discipline are assessed by the chief occupational supervisor.

At the end of the first week the staff meet at a case conference to discuss each new entrant and review others. Gradually as each member of the team gives his opinion a picture of each individual and his capabilities is built up. The unit's rehabilitation officer, who co-ordinates the team's work, then asks the all-important question: "Is this person going to benefit from industrial rehabilitation?" and sums up his or her case. The conference next decides what kind of work the rehabilitee should do while in the unit, and when progress should next be assessed.

The Range of Work

The various workshops are equipped for woodwork, bench engineering, machine-operating, education and clerical work, heavy occupations, and miscellaneous light work, each section being controlled by a skilled craftsman. Much of the work is supplied on contract by outside firms, for it is important that articles produced should have real practical value; trainees are not asked to make things simply for the sake of keeping them occupied. At present they are making aids for the disabled, coat-hangers, mattress springs, heavy garden furniture, bolts, and small household articles. In the education section a trainee can brush up his workshop maths or typewriting, or learn clerical routines.

Whom Can Perivale Help?

Perivale is prepared to cope with a wide range of disabilities. Some 25% of the entrants suffer primarily from mental abnormalities—schizophrenia, anxiety states, personality disorders, and compensation and post-traumatic neuroses. Practically all branches of surgery and medicine are represented: a recent analysis included people with displaced intervertebral disks, limb fractures and amputations, head injuries, hemiplegia, arthritis, coronary ischaemia, poliomyelitis, disseminated sclerosis, epilepsy, chronic bronchitis, tuberculosis, and even lung cancer. Finally a certain number were prevented from holding a job by social afflictions such as language difficulty, domestic stress, alcoholism, or just sheer laziness. Many types have passed through the unit, ranging from doctor, curate, and stock-broker to unskilled labourer, deaf mute, and high-grade mental defective.

The overall success of the I.R.U.s was referred to recently by the Minister of Labour, Mr. John Hare, when he opened a new I.R.U. at Aintree. He said that since the first unit was started at Egham in 1943 another 16, providing in all places for 1,900 people, had been opened in the major industrial centres of Great Britain. Last year 83% of the people admitted had completed courses satisfactorily. Of these, more than 70% were in employment or had entered training within three months of leaving the units.

The unit at Perivale can be of great value to hospitals and general practitioners in its catchment area. Mr. G. H. Cullen, the unit's manager, and Dr. Joseph Lister, its medical officer, would at any time welcome doctors and show them

the unit at work. Case conferences are held on Wednesdays from 11.30 a.m. (Telephone: ALPerton 1451.) Visitors to the unit will see what very practical help it can offer the doctor in rescuing the lame and the unwilling from what Richard Steele called "the insupportable labour of doing nothing."

Nova et Vetera

"BY THE VISITATION OF GOD"

THE DEATH OF JOHN WILLIAM POLIDORI, M.D., IN 1821

BY

HENRY R. VIETS, M.D.

Curator, Boston Medical Library, Boston, Mass.

The circumstances surrounding the sudden death of John William Polidori (M.D. Edin., 1815) at his father's house, 38 Great Pulteney, London, on Friday, August 24, 1821, has until recently remained unclear and the exact cause of death a subject of speculation. Was it suicide at the age of 25, as thought by his family, that brought to an end a promising career in this handsome and talented young man, who had been Lord Byron's travelling physician only five years before?

The following statement, presumably supplied by his father, was published posthumously as an appendix to Polidori's last book, *The Fall of the Angels, A Sacred Poem* (London, John Warren, 1821).[1]

"DR. POLIDORI, after an absence of about three weeks from London, returned the 20th of last August, looking very ill, to his Father's house. He complained of frequent loss of sight, and a pain in his side. On the 24th ensuing, late in the morning, MR. POLIDORI'S servant, not seeing him come out of his room, entered it, and found him in the agonies of death. Medical assistance was procured, but it was too late: he died soon after. His Father, who was in the country, arrived a few hours after the melancholy event, to hear the dreadful and unexpected news of the premature death of a beloved son at the age of five-and-twenty.

"A Coroner's Inquest was held on the ensuing evening, in the presence of a respectable Jury, composed of about twenty persons, who returned a verdict of *Died by the Visitation of God*.

"The rest of MR. POLIDORI'S family, who were all in the country, having returned directly, accompanied the deceased on the 29th to his grave, in the Churchyard of St. Pancras, where his afflicted parent intends to erect a stone with the following inscription:

JOANNIS GULIELMI POLIDORI
M.D.
QUOD MORTALE ERAT
HIC SITUM EST.
OBIIT IX. KAL. SEPT.
A.D.
MDCCCXXI.
AETATIS XXV.
PATER MOERENS
DILECTISSIMO FILIO
HOC MONUMENTUM POSUIT."

The coroner's inquest mentioned in the account was held on Saturday night, August 25, more than 24 hours after death, at his father's house. The jury returned a verdict of "Died by the Visitation of God," thus allowing the body, because of the finding of "natural death," to be buried on August 29 in St. Pancras Churchyard, London, a frequent resting-place for Roman Catholics. Whether or not the stone described in the statement was ever erected cannot now be determined. Owing to a partial destruction of the burial ground, no trace of the grave can be found (1960). The burial, however, is recorded in the St. Pancras Church Register, with the correct name, address, age, and date.[2]

The story might well end at this point, except for some uncertainty in regard to exactly what happened on Friday morning, August 24, and the manner of reaching the favourable verdict by the coroner and his jury. The coroner's records, fortunately, are still available, preserved among the muniments at Westminster Abbey.[3] These documents throw light not only on the exact nature of Polidori's death but also on the method of conducting a coroner's court in the City and Liberty of Westminster in the County of Middlesex in 1821.

The Coroner's Jury

The coroner, John Henry Gell, Esquire, issued a warrant on August 25, the morning after Polidori's death, "for Jury on John Polidori" on the usual printed form for the City and Liberty of Westminster, in the County of Middlesex. It was addressed "To the Constables of the Parish of Saint James within the said Liberty of Westminster."

The hand-written list of the 24 prospective jurors, with names and addresses, is attached to the warrant. The men all lived in the Golden Square region of Soho, seven in Great Pulteney Street itself, where Polidori died, and the other in the immediate neighbourhood.[4] One lived in Golden Square and another in Marlborough Row; none were more than a quarter of a mile from the home of Professor Guitano Polidori at 38 Great Pulteney Street, where the inquest was held at 7 p.m.

The body of John Polidori was viewed, "he then and there lying dead." Witnesses were then heard: first, the two surgeons who had responded to the hurried calls on Friday noon, and, secondly, two residents of the house.

The first witness was Thomas Copeland of Golden Square, surgeon, who deposed on oath:

> "Yesterday about one o'clock I was suddenly called. I went immediately and found the deceased in a front Room on the first floor of this House. He was dressed —he was perfectly senseless and in a dying state. I attempted to discharge the contents of the stomach but ineffectually. He died (I believe) ten minutes after.
>
> [signed] Tho. Copeland."

Thomas Copeland (1781–1855), 40 years of age, had studied at St. Bartholomew's Hospital and qualified as a surgeon in 1804. By 1821 he was an eminent practitioner in London and had already published his pioneer work on diseases of the rectum (1810). He lived only two streets away from the Polidori's at 4 Golden Square. There is no note that he was questioned regarding the cause of death.

The second witness, William Davies, of 59 Poland Street, also a surgeon, testified:

> "I was suddenly called yesterday between 12 and 1 o'clock. I went immediately and found the deceased in the front Room of the first floor of this House—he was in Bed there—He was dead.
>
> [signed] Will^{m}. Davies."

William Davies has not been further identified.

Of somewhat more value is the sworn testimony of the two other witnesses. First came the servant of the household, Charlotte Reed:

> "I am servant here to Mr. Guitano Polidori, the Father of the deceased. The deceased at the time of his death

was aged about six & twenty years. He resided in this House. He has not been very well in health lately. He returned from Brighton on Monday last [August 20]. He did not then seem as heretofore in his behaviour for he then spoke quick & short. Before he went to Brighton he did not appear well in his health. And since his return he has ordered his dinner in such a way as he was not used to do. He dined on Thursday last [August 23] with a Gentleman [John Deagostini] up stairs in this House. He was not in good spirits in the Evening of that day. I saw him about 9 that night. He asked me to leave a Glass (a Tumbler) in his Room. This was not usual, but I left one. He told me he was not well & if he was not up by 12 next day I was not to call him. I went to his room about 10 minutes before 12 to open the shutters. I opened them. As I was returning back I saw he looked very ill. He was in Bed and undressed. He lay in a common position. I soon left the room & told the Gentleman up stairs, who came down stairs immediately. I afterwards went for medical assistance.

[signed] Charlotte Reed."

Finally comes a statement of greater importance, from the roomer upstairs, John Deagostini,[5] who had been quickly called by Charlotte Reed.

"The deceased dined with me in this House last Thursday [August 23]. He accepted my invitation in an abrupt way. This had been usual with him for some time and for the last 2 years when he had an accident & was thrown from his Gig and hurt on the head. He spoke on Thursday in half sentences in conversing on politics & future time. He said I should see more than him. This was said in a very harsh way, before he left Table & shook the Gentleman in our company by the hand so violently that it forced him to kneel. The deceased appeared deranged in his mind and his countenance haggard. He ate but little at Dinner. We parted but he joined us again at Tea when he hardly spoke a word. He left us about 9 that night. Next day [August 24] after Breakfast I enquired of the Maid if he had gone out. She replied No & that he had desired her not to call him. She came up to me much alarmed about 12. I went down immediately into his Room. There was a Tumbler on the chair. This contained only water. I did not observe in the room the remains of any deleterious substance. He was senseless and apparently in a dying state. Dr. Copeland drank part of the water in the Tumbler.

[signed] John Deagostini."

The testimony of the four witnesses, written by the clerk but signed by each, ended the inquest. There is no indication of a post-mortem examination or an investigation of the material agents, such as the tumbler. The possibility of poison in the room where Polidori died was not, so far as the record shows, given consideration, except for the observation of Deagostini. The verdict was that "the said John Polidori . . . departed this Life in a natural way by the visitation of God." The document is signed by J. H. Gell, Coroner, and all twelve jurors.

The Question of Suicide

The judgment of the coroner's jury was decisive. The death, pronounced in unmistakable terms, was a "natural one." But the family, both at the time and later, considered otherwise. His nephew, William Michael Rossetti, editing Polidori's *Diary* nearly one hundred years later,[6] wrote: "In August 1821 he [Polidori] committed suicide with poison—having, through losses in gambling, incurred a debt of honour which he had no present means of clearing off. That he did take poison, prussic acid, was a fact perfectly well known in his family; but it is curious to note that the easy-going and good-naturedly disposed coroner's jury were content to return a verdict without eliciting any distinct evidence as to the cause of death, and they simply pronounced that he had 'died by the visitation of God.'"

One notes, however, that no mention of prussic acid occurs in the dispositions by the doctors, and, if Deagostini's statement can be taken as truthful, Dr. Copeland actually drank part of the water in the tumbler left sitting on the chair beside the dead Polidori. Such an act would appear foolhardy if Copeland, a man of substance, considered the tumbler had contained a rapidly acting deadly poison. This act confirmed Deagostini's testimony that the tumbler "contained only water." In this exchange one glimpses the idea that suicide was naturally suspected from the condition of the dying or dead man, but Copeland, a most competent observer, dismissed the idea, at least so far as the tumbler was concerned.

Copeland states, in addition, that Polidori died ten minutes after he was first seen by him, about one o'clock or shortly after. As Charlotte Reed, the servant, had found him "very ill" at ten minutes before twelve and Deagostini reported him "senseless and apparently in a dying state" a few minutes later, if prussic acid had been taken it would be surprising for Copeland to have found him still living an hour or more after Charlotte Reed's discovery. Prussic acid seems an unlikely agent if suicide was attempted. Some other, more slowly acting poison may of course have been used. But it is at least uncertain that any form of poisoning was the cause of death. Indeed, there is some evidence that symptoms of nervous instability had existed for a year or longer, possibly of importance in evaluating the terminal event.

Deagostini, living in the same house with Polidori, had noted some abruptness of speech occurring subsequent to an injury two years before death, when the young doctor was thrown from his gig and was "hurt on the head." Such a behavioural change might well have been a sequel to cerebral trauma.

A harsh way of speech, "in half sentences," violent actions, and a haggard countenance, were also noted by Deagostini as more immediate symptoms the night before death. Polidori ate little at noon and hardly spoke a word at tea before he retired to his room at nine. And yet Deagostini could not have suspected impending suicide, for he expected Polidori to leave the house by himself the next morning, and indeed inquired of the maid at breakfast if he had done so.

The maid, too, had noted some change in Polidori. He had "not been very well in health lately," and when

[1] Another edition by the same publisher, but without Polidori's name, was issued before his death in 1821. The posthumous edition has Polidori's name on the title-page, and carries the death notice and a list of his published works.

[2] By courtesy of Mr. K. S. Gladstone, Acting Vestry Clerk, St. Pancras Church, who searched the records for me (1960).

[3] The coroner's inquest reports were made available to me through the kindness of Mr. Lawrence Edward Tanner, Librarian, Westminster Abbey Library, London.

[4] R. Horwood, *Plan of the Cities of London and Westminster . . . shewing Every House*. London, 1792–9.

[5] John Deagostini, a scholar and family friend, lived in an apartment on the upper floor of the Polidori house. John Polidori dedicated his M.D. Edinburgh thesis (1815) to him.

[6] *The Diary of Dr. John William Polidori, 1816, Relating to Byron, Shelley, etc* Edited and elucidated by William Michael Rossetti. Elkin Mathews, London, 1911.

he returned from Brighton on August 20 "he did not then seem as heretofore in his behaviour for he then spoke quick and short." Even before he went to Brighton her master's son had not appeared to her "well in his health." He ordered his dinner in an unusual manner and actually told the maid that he was not well and did not expect to be up before noon of the following day. If suicide was being considered by Polidori when he retired one would have expected, moreover, the attempt to have taken place at the usual time, the early morning hours, and not postponed until noon.

Was he dead when found? The maid reported he "looked very ill" at ten minutes to twelve. She does not say he was dead. Deagostini, a few minutes later, found him "senseless and apparently in a dying state," but presumably not dead. When Copeland arrived, probably an hour later, he found Polidori "senseless and in a dying state." He certainly was not dead, for Copeland "attempted to discharge the contents of the stomach," an action he would not have done on a dead body. But Copeland was even more definite in his testimony when he stated: "He died (I believe) ten minutes after." By "after" I presume he meant ten minutes following the attempt at emesis, but there seems some doubt in his mind as to the exact time. The important point is he found Polidori alive. If the maid ran to Copeland's house on Golden Square and the doctor came back with her on the run, the elapsed time can hardly have been less than a half-hour, perhaps longer. Such an interval of time is inconsistent with prussic acid as the cause of death.

Polidori's death notice was reported in *The Traveller* (London) on Monday evening, August 27, 1821,[6] but the report on the inquest was not published until September 11 in the *Morning Chronicle*, *The Courier*, and the *New Times*. Each of the inquest newspaper accounts refers to the coroner, for some unknown reason, as T. Higgs, not J. H. Gell, who actually signed the document.

One can only conclude, therefore, that the verdict of the coroner and his jury was justified. Suicide, by prussic acid or other means, was "not proven." There is no evidence in the documents of the coroner's inquest to uphold the validity of the statement by Polidori's nephew, William Michael Rossetti, that the young physician did take a poison to end his life.

A BIOGRAPHICAL VALHALLA

This new volume of *The Dictionary of National Biography** records the lives of 725 men and women who died in the decade 1941 to 1950. The contributors are writers of distinction and for the most part have personal knowledge of the person commemorated. The editors have ably performed a difficult task, and, though omissions will be noted, few will criticize those chosen for admission to this biographical Valhalla.

Here the medical profession receives a due share of posthumous honour. Of the 13 physicians, the doyen, Sir Thomas Barlow, who died in his hundredth year, heads the list. Then comes Sir Farquhar Buzzard, neurologist and regius professor, who saw Oxford medicine expand into a clinical school through the munificence of Lord Nuffield. The life of Lord Dawson of Penn, the statesman of medicine, is ably recorded by his daughter, Lady Eccles. Next come Sir William Hale-White; Sir Thomas Lewis, the famous cardiologist; Sir Walter Langdon-Brown; Sir Thomas Oliver, an authority on industrial hygiene; Sir Humphry Rolleston, clinician, pathologist, and medical historian; John Ryle, a great clinician and a pioneer in social medicine; and Sir Frederic Still, the first to specialize in children's diseases and the discoverer of Still's disease. With him ranks another eminent paediatrician, Sir Leonard Parsons, of Birmingham. Sir William Willcox, who combined medicine with toxicology, is aptly described as "the most deliberate and painstaking expert witness," and Warrington Yorke is renowned for his work in tropical medicine.

The casualty list of pathologists and bacteriologists is also a heavy one. Here are lives of Sir Joseph Arkwright, who made fundamental researches on bacteriological variation; William Bulloch, bacteriologist, pathologist, and medical historian; Sir John Ledingham, whose researches advanced knowledge of bacteriology, pathology, haematology, immunology, and virus diseases; Sir Bernard Spilsbury, "the leading detective-pathologist of the day"; Professor Topley, a brilliant investigator; and, last but not least, Sir Almroth Wright, who ranks, says his biographer, Leonard Colebrook, "with Pasteur, Ehrlich and Metchnikoff among the founders of modern immunology."

The surgeons were also men of fame. There are those two great pioneers in orthopaedic surgery, Sir Henry Gauvain and G. R. Girdlestone; Sir D'Arcy Power, whose work as a medical historian went hand-in-hand with surgical skill; Sir Harold Stiles, of Edinburgh; Sir Cuthbert Wallace, whose surgical knowledge was employed in the South African War and in two world wars; and Sir William Wheeler, the Irish surgeon, a brilliant operator.

Sir Frederick Gowland Hopkins explored the chemistry of intermediate metabolism and established biochemistry as a separate discipline. Three dermatologists may be mentioned. Of these J. H. Sequeira introduced Finsen light treatment into England; Sir Norman Walker was also an administrator and an able president of the General Medical Council; Sir Ernest Graham-Little, after establishing an international reputation in dermatology, represented London University in Parliament. Physiology is personified by Sir Frederick Banting, whose discovery of insulin with Best is recorded by Best himself; and by Sir Joseph Barcroft, famous for his work on haemoglobin, respiration, and other problems. Sir Arthur Newsholme, medical officer of the Local Government Board; Sir George Newman, chief medical officer of the Ministry of Health and Board of Education; and Sir Frederick Menzies, chief medical officer of the London County Council, contributed their gifts to administration and progress in the field of public health.

C. S. Myers illuminated experimental psychology, and two alienists of distinction, Sir Hubert Bond, of the Board of Control, and Sir Robert Armstrong-Jones, are also here. The late Sir Drummond Shiels has written a sympathetic account of a general practitioner, H. A. Moody, a Jamaican practising in Peckham, who founded the League of Coloured Peoples.

Other lives also will interest medical readers. Tom Jones's studies of Earl Baldwin and Earl Lloyd-George are superb. Under John Burns and Sir Horace Monro the national tuberculosis and child welfare services were organized by Newsholme. C. S. Gibbon did much for housing and public health. Sir Arthur Robinson, of the Ministry of Health, planned the Local Government Act of 1929, which at long last achieved poor-law reform. Sir Malcolm Delevigne, of the Home Office, is memorable for his crusade against too-easy facilities for drug addiction and for subsequent legislation on the subject. Mrs. Bedford Fenwick and Dame Rosalind Paget were pioneers in nursing reform. Sir Herbert Barker, manipulative surgeon (unqualified), is not forgotten. Those interested in zoology will appreciate the lives of Sir D'Arcy Thompson, Sir Edward Poulton, and that modest genius Professor E. S. Goodrich. This volume of the *D.N.B.* well maintains the high standard of its immediate predecessors.

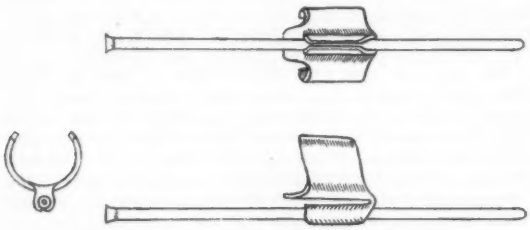
**The Dictionary of National Biography, 1941–1950.* Edited by L. G. Wickham Legg and E. T. Williams. (Pp. 1,031+xxi. £5 5s.) Oxford University Press. 1959.

Preparations and Appliances

NEEDLE DIRECTOR FOR PUDENDAL BLOCK ANAESTHESIA

Mr. H. COHEN, Redhill County Hospital, writes: The advantages of pudendal block anaesthesia over general anaesthesia for obstetric procedures have been discussed in many recent articles. It is safe, simple to carry out, and suitable for nearly all vaginal manipulations.

The method described in most textbooks involves local infiltration of the skin around the vagina and blocking the pudendal nerve on each side by an injection through the perineum. The transvaginal method was originally described by Kobak, Evans, and Johnson (1956) and more recently by Huntingford (1959). In this technique the needle is guided into the vagina by the right index finger to block the right pudendal nerve and the left hand is used for the



opposite side. The one disadvantage of this method is that the needle tends to catch in the rubber glove or, worse still, the finger, particularly if the presenting part is low in the pelvis. A simple introducer overcomes this disadvantage and enables the spine and nerve to be found with unfailing accuracy.

The needle director consists of a finger-clip combining a slideway along which a directing sheath may be moved (see Diagram). The needle director is used in the following manner. It is clipped to the inside of the second finger and the directing sheath is adjusted until the proximal end is approximately 1½ in. (3.8 cm.) across the palm of the hand. With the patient in the lithotomy position the ischial spine may be accurately located by the directing sheath nose per vaginam. Injection is then carried out by sliding the needle down the inside of the directing sheath into the subepithelial tissue. The same or opposite hand may be used for the other nerve.

The instrument is simple and may be obtained with a fixed or adjustable clip. It is made by Messrs. A. F. Harding, Surgical Instrument Designers and Manufacturers, 3a Clarendon Road, Redhill, Surrey.

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(*Continued from next column*)

that its spasm-producing properties are inferior and its duration of action less than that of ergometrine, so that delayed haemorrhage is more likely. For this reason it has been suggested that the injection of oxytocin should be followed up with intramuscular ergometrine.

The new preparation, syntometrine, provides in convenient form an oxytocic for intramuscular injection (which is therefore suitable for routine use by midwives) combining the rapid action of oxytocin with the more sustained action of ergometrine. A preliminary report[1] on it recently showed that "experience in the first 46 cases has been encouraging."

N.H.S. Basic Price.—1-ml. ampoule, 4s.

REFERENCE

[1] Embrey, M. P., *Brit. med. J.*, **1961**, **1**, 1737.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Ergometrine with Oxytocin

"Syntometrine" (Sandoz).

Composition.—This preparation consists of a stable solution containing 0.5 mg. ergometrine maleate *B.P.* and 5 units of synthetic oxytocin ("syntocinon").

Pharmacology.—More than a score of natural and semi-synthetic alkaloids have been isolated from crude ergot. They all share a common structural component based on lysergic acid, but only the laevo-rotatory members of the group are pharmacologically active, possessing oxytocic as well as sympatholytic and other less important actions. Ergometrine is the best-known and clinically the most important ergot alkaloid because of its outstanding oxytocic properties.

The two active principles yielded by the posterior pituitary gland—oxytocin and vasopressin—have until recent years been available only in the form of somewhat impure extracts. In 1949 oxytocin was isolated in pure form, but not until 1953 was its chemical structure elucidated as a cyclic polypeptide amine and the hormone finally synthesized. It is now available commercially as syntocinon.

Ergometrine increases uterine contractility strikingly; 0.5 mg. intramuscularly causes a powerful tetanic contraction of the pregnant uterus lasting some three-quarters of an hour, after which the spasm gives way to intermittent large contractions for two to three hours. Oxytocin, too, is a powerful stimulant of uterine contractility and increases the amplitude and frequency of uterine contractions. It is sometimes said that oxytocin, unlike ergometrine, does not produce tetanic contraction, but the difference is one of degree only. The larger doses of oxytocin (for example, 5 units) produce considerable if comparatively short-lived (15 to 20 minutes) spasm, the total effect lasting about 30 minutes.

Therapy.—The administration of an ergot preparation to control uterine haemorrhage after the end of the third stage of labour has long been established practice. It is only in relatively recent years, however, that injection of an oxytocic before the birth of the placenta has been viewed with favour. Nowadays not only is the injection of ergometrine advised for the treatment of haemorrhage in the third stage, but in many units it is given routinely as soon as the head is delivered in order to expedite delivery of the placenta and reduce considerably the incidence of post-partum haemorrhage.

The quickest effect (in less than 1 minute) is obtained by using ergometrine intravenously, but because midwives are not normally trained to make intravenous injections the routine use of the intramuscular injection has been advocated, and its much greater applicability has led to its general acceptance in many hospitals. The addition of hyaluronidase to the intramuscular injection to accelerate its speed of action has recently been claimed to be advantageous.

It has been shown that the mean time between injection of ergometrine + hyaluronidase and uterine response is approximately 4¼ minutes. This compares favourably with a latent period of about 7 minutes for intramuscular ergometrine but is still much lower than the intravenous injection.

Oxytocin (given intramuscularly) has the merit of acting more quickly than intramuscular ergometrine, being effective in about 2½ minutes. But it has not been much used in Great Britain chiefly because in the past injection of the older pituitary extracts was occasionally followed by profound shock. Oxytocin, moreover, has the drawback

(*Continued at foot of previous column*)

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Vaginal Pessaries

SIR,—I read with astonishment Professor James K. Russell's categorical statement (December 16, p. 1595) that there is no place in modern gynaecological practice for vaginal pessaries in the management of prolapse. Surely it is better to treat prolapse in the young patient desirous of having further pregnancies with a pessary until her family is complete. There will always be some patients who adamantly refuse to undergo a surgical operation, and it would be wrong to withhold pessary treatment if this renders them comfortable. Further, in spite of Professor Russell's assurances, surgical operation is not without danger to life, particularly in those recognized as poor surgical risks. Even the relatively minor Le Fort operation, in the writer's experience, has been followed by a fatal pulmonary embolism.

Unfortunately, Professor Russell has not indicated the nature of the ring pessaries used in the cases he describes, but I should imagine they were of the vulcanite or rubber watch-spring variety—both bound to become eroded by the vaginal secretions after prolonged use and so lead to mechanical irritation. I am sure that if such pessaries are avoided and the modern plastic type used instead much less vaginal-mucous-membrane irritation will be caused, and the incidence of "pessary" carcinoma of the vagina thus fall to a negligible level.—I am, etc.,

Midwifery Department,
Foresterhill,
Aberdeen. J. F. B. WYPER.

Clinical Responsibility

SIR,—A doctor who has completed his training and become finally established is completely responsible for his patient, including, when necessary, the decision to refer him elsewhere for further advice. This implies a trust, not in his unlimited skill, but in his ability to recognize his own limitations. This, surely, should be the clinical responsibility to which Dr. H. B. Hewitt refers (November 25, p. 1428).

Many of the frustrations alleged against the N.H.S. arise from a failure to appreciate the importance of this principle of full clinical responsibility. A professional man expects to follow his chosen profession without direction, interference, or control in professional matters. To deny him this right and duty is to degrade him in his own eyes to a form of technician. He expects to be supervised as a student and as a junior in training, but, once he is established, he will greatly resent supervision. It follows that a very important function of a medical school is to impart to the student the ability to recognize the limitations of his own knowledge and sphere of activity. It is by the exercise of a humble conscience that he will decide whether the needs of his patient require him to call in help.

The problems caused by this concept are largely emotional but, none the less, real. The S.H.M.O.'s grievance was surely due, not simply to pay, but also to the rule that all beds must, in theory, be consultant beds and that in some degree he had no patient he could call his own. He was thus, if only in theory, supervised.

The G.M.S. Committee states that the G.P. returning to hospital is used to clinical responsibility and expects to keep it. The new medical assistant grade is therefore under suspicion because of the feeling that a doctor who may accept supervision whilst under training should not have to do so throughout his professional life. Similarly the G.P. resents supervision in the obstetric field by a consultant and is surprised to find that his "revised terms of service *require* (my italics) a doctor to base his services on the principles set out in the Memorandum on Maternal Care . . ."[1]

Worse than all this, however, has been the tendency to divide the profession into the G.P. who is expected to know nothing and refer everything and the consultant expected to know everything and refer nothing. The deliberate referral of cases lying within a doctor's capacity—even if due to pressure of work—at first grates on the conscience and later, by repetition, tends to injure or destroy professional integrity. But the plight of the consultant is little better. From the moment of his appointment he is expected to deal fully with every case within his specialty. How seldom does he write back to the G.P. to say that his experience of a case is inadequate and to recommend its reference to a more experienced consultant? Financially, the merit award system may recognize that one man is twice as valuable as another, but clinically the subject is not only taboo but secret. Even the G.P. with a very difficult case cannot find out whom the consultants themselves regard as outstanding!

Reference to the *Report on Confidential Enquiries into Maternal Deaths 1955–1957* shows that final clinical responsibility for avoidable deaths lay on the consciences of 25% of consultant obstetricians (116 amongst 426 consultants) but only 1.3% of G.P. obstetricians (172 amongst 14,000). Consultants who shoulder this great burden should not be inhibited by custom or administrative difficulty from referring their difficult cases to colleagues of a higher grade, nor should they be forced to delegate to juniors in training cases sent to them as needing consultant care.

A clear understanding by everyone of the principles underlying full clinical responsibility would go far towards solving many problems, including that of medical emigration. It is also time to reconsider whether the names of recipients of merit awards should not be published. Degrees and fellowships indicate only the basic equipment at the start of professional life. How much more important it is to publish a man's grading based on his colleagues' assessment of his skill and faithfulness in applying his art. Both G.P. and patient have a right to full knowledge of the consultant whose advice they seek.—I am, etc.,

Holywell, Flintshire DAVID L. WILLIAMS.

REFERENCES
[1] *Report of the Ministry of Health for the Year Ending 31st December, 1960*, 1961. Part I. Ministry of Health, London.
[2] *Report on Confidential Enquiries into Maternal Deaths in England and Wales, 1955–1957*, 1960. Ministry of Health, London.

Nationalities of Junior Staff

SIR,—I have just received my copy of the *Journal* for October 28 which contains at p. 1148 the admirable letter on this subject from Professor Charles Wells. As the majority of the postgraduates now staffing the hospitals

of the United Kingdom come from India and Pakistan, I wish to say how the situation appears from here.

I would support Professor Wells's suggested scheme of recruiting registrars into one central pool, not only for the reasons he gives but also for the good name of British institutions. So many Indian doctors return to their own country after a period of "training" in the United Kingdom with a sense of grievance, because to all intents and purposes the doors of the teaching hospitals are closed to them when it is a matter of making appointments to the junior staff. They go to Great Britain for training which, for the present, they cannot easily obtain in their own country, only to find that the hospitals which train British doctors will not have them except as fee-paying students. It is rare even for an Indian to be short-listed for a post in one of these places, whatever his qualifications. It is not difficult to imagine the feelings of an Indian doctor with higher qualifications obtained in Britain when he hears, as they sometimes do, that the first step in compiling a short-list is to exclude all Indians and Pakistanis.

The teaching hospitals are the worst offenders, but there are other hospitals which apparently pride themselves on never entertaining applications from doctors from these Commonwealth countries. Snobbery is an ancient British vice which the natives of the country may accept with a shrug, but which is most offensive to strangers. It flourishes remarkably in many of our "better" hospitals.

These automatic exclusions on grounds of race are not only offensive, they are also foolish since the persons excluded are of high intelligence and know quite well what is going on. The resultant bitterness does a real disservice to our country. It must also be remembered that postgraduate medical education in India is developing rapidly, and it may not be long before we have to offer attractive terms to Indian postgraduates if we are to get them in any numbers. The prospect of an appointment at a teaching hospital is the kind of inducement that will attract them; and the scheme proposed by Professor Wells seems a sensible way of providing this. I hope it will receive serious attention.—I am, etc.,

Sarojini Naidu Medical College, Agra, India. DUNCAN MACAULAY.

SIR,—Mr. N. S. Banerji's comments (November 18, p. 1356) will appear remarkable to Asian doctors like myself who have been recently in the U.K. and who, on the whole, will remember with nostalgia the hospitality, cordiality, and, what is naturally more important, the training they received. I was therefore considerably surprised at the words "untrained and unfit" that Professor Charles Wells (October 28, p. 1148) was supposed to have used and at which Mr. Banerji took umbrage. On re-reading Professor Wells's letter and the context in which they appear, I note that Professor Wells said: ". . . the great majority of registrars in the smaller, most isolated, peripheral hospitals were Asians. This [arrangement] cannot be regarded as satisfactory since these men, often working by themselves, are frequently called upon to shoulder responsibilities for which they are (through no fault of their own) untrained and unfitted." This is in the context of the comparative postgraduate educational status of these doctors—a subtle difference. It should be obvious, too, that if foreign doctors *were* trained they would not go to the U.K. from their country, and Professor Wells *does* point out that the Asians were doing jobs they were unfitted for, not unfit for.

The growing resentment against foreign doctors on which Mr. Banerji comments is very likely in view of the increasing influx of, for example, Indo-Pakistan medicos. (Mr. Banerji might be cheered to learn that when I was in the U.K.—1953 to 1958—there was quite a "hate" on against Irish doctors in the average doctors' mess.) I should also imagine that the recent Immigration Bill has confused the issue further or at least has led to some spirited arguments during "elevenses."

As the Sheffield Regional Hospital Board (October 7, 1961, p. 950) has taken the trouble to analyse statistically the question of the employment of overseas doctors as registrars, it might be well at this stage to remember a recent parallel. In the U.S.A. a tremendous influx of good and bad foreign doctors without adequate screening flooded the U.S.A. under the Exchange Visitors Programme, and the abuses of the system—by the bad doctors—resulted in the examination of the Educational Council for Foreign Medical Graduates. This caused much bruised feeling, bitterness, and unpleasantness all round, and several good men left the U.S.A. in disgust. A thoughtful stocktaking in the U.K. is essential right now before a similar measure may have to be introduced, splitting up the Commonwealth medical profession, or we, the Commonwealth medical profession, and our medical standards might have to contend with something roughly on the lines of the recent Immigration Bill.

It is not for those who have been guests in the U.K. to comment on its National Health system and the registrar/consultant bottleneck it produced, which resulted at one time in such an exodus of disillusioned young British ex-registrars to Canada and Australia. But this much-discussed problem, and that of foreign registrars and their medical education, training, and supervision, does require urgent and thoughtful reappraisal. Both are interrelated to a great extent, and I am sincerely glad to read of Dr. J. D. Hennessy's suggestions (November 18, p. 1356) regarding the former, the statistical survey of the Sheffield Hospital Board regarding the latter, and Professor Charles Wells's constructive suggestions to solve both problems at one stroke and equalize any imbalance between indigenous and overseas men, with fairness at all levels.—I am, etc.,

Bombay 8, India. LESLIE DE NORONHA.

"A Pretty Ghastly, Awful Picture"

SIR,—In these days of unreality no doubt you are right (December 9, p. 1548) in regarding Dr. J. R. Seale (p. 1554) as bold to state the obvious: namely, that young men are finding the conditions of service in the N.H.S. unattractive and they show it by their actions.

From among the mass of reports and theories to which you refer in your leading article one fact seems to me to stand out as equally obvious: whereas 4,000 foreign doctors find it worth their while to hold junior hospital posts in order, as you rightly say, to gain experience, yet young English doctors do not. The reason for this must surely be that the experience gained in these posts will not, by and large, be of value to doctors who propose to practise in England. Why not? The experience that the foreign doctors regard as so valuable is mainly that of minor surgical or medical procedures and familiarity

with such basic diagnostic aids and techniques as are available in casualty departments. When they return to their own countries they aspire to equip themselves with these facilities and to practise the techniques they have learnt. Their social and financial rewards will be in proportion to their skill and success in so doing.

British doctors entering general practice under the N.H.S. see no such prospect before them. The cult of the specialist and of the hospital, the need to avoid legal liability by passing the buck and sharing responsibility, and the capitation system of remuneration that puts a premium on numbers of patients rather than on quality of service, all discourage the exercise of technical skills by general practitioners. Even the public now hardly seems to expect it of them. So why trouble to learn them? The patients will readily agree to go to hospital, if in fact they have not already gone there on their own account to swell the number of trivial or purely social problems that crowd the casualty and out-patient departments and the wards too.

The fortunes and hardships of the relatively few young men who are so interested in a specialty and so determined against all discouragement that they hang on in a subordinate hospital post, so as eventually to become a consultant, are well known to their juniors and students, who are little encouraged thereby to follow the same road. That, in my belief, is the answer to the question. So what should be done about it?

The first thing is to decide whether family and general practice is to be the root of the Health Service with the hospitals an accessory extension of it, or vice versa. Maybe the rising generation will think the latter is the better way. It is clearly the way things are now tending. If, on the other hand, general family practice is to be the main trunk from which the hospitals and other branches of the Service spring, then general practice needs radical cultivation at its roots and the branches need drastic pruning to preserve balance and proportion.

I doubt whether any long-term policy such as this reformation would demand could ever be carried through by a series of Ministers of Health of varying political creeds who on average change every year or two. It follows that the Health Service should come under a permanent and non-political organization such as the University Grants Committee. General practitioners must work as teams from properly equipped health centres. The teams should contain members with special qualifications or interest in medicine, surgery, or obstetrics and be provided with the equipment they need. Like any successful team the group must have a head. Capitation fees as the system of remuneration in such an organization would be impossible. Though I instinctively distrust and dislike it, a whole-time salaried basis seems the only possible alternative. Salaries would be based on a scale related to special qualifications, experience, and conditions of place of work. Vacancies would be filled by advertisement and application. The College of General Practitioners would be vital to this scheme and its diplomas necessary for acceptance for qualification in the higher grades. Private, free-lance practice must be recognized as essential and complementary to the salaried service. A fair method must be devised whereby N.H.S. doctors could commute their pensions and strike out in private practice, or private practitioners could be free to apply for vacancies advertised in the N.H.S. Hospital service would, of course, be free equally to the patients of all doctors.

This is not the first time I have put forward the views here so briefly outlined. They proved extremely unpopular with nearly all concerned, politicians and doctors alike. Maybe that in contrast to the "pretty ghastly, awful picture" that now confronts us they may not appear so outrageous, and may even provide a new and helpful line of thought.—I am, etc.,

Plymouth, Devon. W. A. LISTER.

SIR,—Many of us have been firmly convinced for some years now that increasing staffing problems were going to beset the medical profession, but because on our side we were not so statistically inclined the Willink Committee gospel was accepted by the Government, laughable as many of us then knew it to be. When at last a glimmer of the truth is appearing (December 9, p. 1548), there still seems to be no full-blooded effort to tackle the problem at this present time.

The Platt Committee[1] has high-lighted some of the problems, especially in hospital staffing, which position should slowly worsen; and do not expect the general practitioner to fill in the gap, because it will not be practicable. In any case the latter is about to develop a fearsome migraine trying to combat his own G.P.-shortage, which is also just beginning to show itself. In my own branch at this time the early cracks of trouble are showing through the plaster. The Government sooner or later will have to face the fact that until they can afford to put more money into the medical service to allow for the necessary increase in manpower they will get an ever-increasing problem. This problem is incidentally only one of the late results of a too-hastily-inaugurated N.H.S. in 1948 by the politicians. Also the medical schools will have to cater for expansion in both students and staff to teach them. Lastly the profession itself needs to utilize its own manpower more efficiently. It is therefore easy to see why the medical services may face a partial breakdown within a few years.

I suggest that realistic and determined action take place immediately, jointly between the Government and the profession, in close unity and purpose, or else there is going to be a frightening problem before the close of the '60s.—I am, etc.,

Cheadle, Cheshire. C. SHIERS.

REFERENCE

[1] *Brit. med. J., Suppl.*, 1961, **1**, 99.

SIR,—Your leading article (December 9, p. 1548) reports and comments on Lord Taylor's speech in the House of Lords (p. 1578). With due respect I submit that this and previous reports miss one of the main reasons why so many of the young doctors emigrate. To borrow a phrase it can be simply stated as guaranteed employment. Far too many British graduates find that 10 months' employment per year is about the average.

One of the reasons for this is the influx of the 4,000 doctors mentioned in the leader. The doctors compete on equal terms with our own graduates and are prepared to take posts junior to their years of qualification and paper qualifications. They are quite prepared to do this since they will only stay a short time. As a result we see British graduates refused posts in preference for foreign doctors whose qualifications and experience exceed those required for the post. One recent junior medical appointment in London attracted

over 60 applications. This problem could be met by not allowing any temporary immigrant to take a post unless there was no suitable British graduate.

The rural hospitals will not get applicants for posts as long as preference in future appointments is given to teaching-hospital doctors. The present level of litigation and the attitude of the courts account for the acute shortage of casualty officers.—I am, etc.,

Stanmore, Middlesex. A. W. WARLTIER.

SIR,—I am writing to congratulate you on your leading article on "a pretty ghastly, awful picture" (December 9, p. 1548). It is rather sad to think that it is only in December, 1961, that this has appeared and not 10 years earlier. At least it is a step forward: the first step to freedom, I suppose, is the realization by the slave of the chains which fetter him.

Contemporaneously with your leader we have received the news that the College of General Practitioners is introducing an examination for future entrants, and that a Membership of the College is being set up. While one has sympathy with the ideals of the College, surely the first step in priority is to remedy "the pretty ghastly, awful picture." The College seems to be putting the cart before the horse with a vengeance. Improving general practice under present conditions is like insisting that a miner at the coal face should wear a white overall. The picture of "Membership" awards being awarded to each other is not a very pleasant one to contemplate.—I am, etc.,

Middleton, Lancs. B. HIRSH.

SIR,—I would like to applaud the analysis made by Dr. J. R. Seale (December 9, p. 1554) of the supply of doctors in this country, and the remarks made in your leading article (p. 1548) on the same subject. As one who has ventured overseas I would like to add some personal comment.

I left England five and a half years ago, and returned a year ago for a period of postgraduate study. I shall not, however, be staying. There are many reasons for this, a lot of them non-medical, for it does not take long to build ties of affection to a country such as New Zealand. My children were born there and my decision must naturally be influenced by what I think the future could hold for them as citizens of either country, as well as by what I can offer them as a parent by my choice of home and work.

Nevertheless an important reason for leaving is a profound dislike of the system of medicine that exists here, together with a disinclination to accept the unsatisfactory rewards which it offers. A great deal of unfortunate experience confirms the unwisdom of accepting the State as a monopolistic employer, and it is quite obvious that a doctor is not yet as valued here as most of us would expect. One can either lump it or leave. Certainly complaint has little effect, and successive Governments have relied upon the improbability of any collective action in their dealings with the profession. Perhaps they will be forced to realize that individual action can eventually have as great an effect even if it is less dramatic.

An increase in the student intake can only be small and ineffective. If sufficient satisfactory students were available for a large increase it is unlikely that the Government would show any more enthusiasm for building new medical schools than it has already for building new hospitals, even in the huts which Lord Taylor suggests (p. 1578). As a solution to the problem it certainly smacks of trying to fill a very leaky bucket. The most to be achieved this way is more young men with a useful passport to successful emigration, and more medically trained young mothers anxious to stay at home.

The Health Service has the depressing and decrepit aspects of premature age, and the only real solution lies in its complete reorganization, and above all in freeing medical practice from its political bondage. Without such changes the exodus will certainly continue. But I suspect that little will be done until the pressures of near collapse are much greater, and the "pretty ghastly, awful picture" will drag on with more years of unhappy wrangling between medicine and politics. I am very thankful to be no longer involved.—I am, etc.,

Southend-on-Sea, Essex. A. G. SLARK.

The Case of the Plastic Surgeons

SIR,—I have read with interest your leading article of December 2 (p. 1483) and also the letter of Dr. H. B. Kidd (December 16, p. 1641) in reference to the "Case of the Plastic Surgeons." The following story may be of interest to your readers.

During the illness of Sir Peter Freyer in 1920 he told a colonel of the Marines living at Deal, who was an old patient of his, to consult me. Some time previously he had had his prostate removed by Freyer, and now merely wanted to be assured that all was well. I asked him who was his general practitioner. He said that he and the local doctor were on bad terms with each other for the following reason:

The colonel had consulted him for dysuria and had been given a prescription. As the difficulty of micturition increased, the patient suggested that a second opinion was needed. The doctor thought otherwise.

Having heard of Freyer from a friend, the colonel consulted him and in due course had a successful prostatectomy. As soon as the patient was convalescent he returned to Deal and sent for his G.P. His first words to the doctor were, "I am quite well now." "Ah!" said the G.P., "I felt sure my medicine would cure you." "No," said the colonel, "I have been operated on by a man named Freyer." "What!" said the G.P. "Do you mean to tell me you consulted that quack?"—I am, etc.,

London N.W.11. CLIFFORD MORSON.

Thalassaemia in Britain

SIR,—Most of the Cypriot population of London lives in the vicinity of the Middlesex Hospital. In the past year we have been struck by the large number of these people attending the medical clinics with pain in the right or left hypochondrium. The letter (November 11, p. 1289) of Drs. R. M. Bannerman and Sheila T. Callender mentioning the frequency of such pain in patients with thalassaemia prompted us to reconsider the cases we have seen, in many of whom no satisfactory diagnosis had been made.

We reviewed all 38 new Cypriot patients seen since December, 1960, in the Medical Unit, one of the six clinics which deal with general medical cases. Eighteen of them complained of pain in the hypochondrium. The remainder had a wide variety of complaints and included

known cases of thalassaemia who did not have upper abdominal pain. The 18 patients with pain were screened for thalassaemia. We also recorded the results of cholecystograms and barium meals, where performed, and also whether the patient was obese. Four cases were found to satisfy the criteria of thalassaemia minor, as shown by the film appearances, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, corpuscular fragility, and haemoglobin electrophoresis. None of the 18 patients was anaemic. In 13 out of 18 patients the pain was right-sided ; in only one of these was thalassaemia found. Of the five patients with left-sided pain, three had thalassaemia. The probability of this association occurring by chance is between one in 20 and one in 50. Of the 13 patients with right-sided pain, six were obese. One case of gallstones (non-pigment) was found by cholecystography, and in three instances barium meal showed gastro-intestinal abnormality.

The results of this small series support the contention of Drs. Bannerman and Callender that thalassaemia may often be implicated in cases of left hypochondriac pain. The association of right-sided pain with thalassaemia is, on our figures, less common. We remain impressed both by the frequency of right hypochondriac pain in this population and by the difficulty in reaching a diagnosis.

We acknowledge with thanks the permission of Professor Alan Kekwick to study patients under his care. The haematological investigations were carried out in the Bland-Sutton Institute of Pathology.

—We are, etc.,

ARTHUR S. E. FOWLE.
G. J. R. MCHARDY.

Department of Medicine,
The Middlesex Hospital,
London W.1.

Corticosteroids in Asthma

SIR,—The opinions expressed on this subject in recent correspondence in the *Journal*, apart from Dr. Richard Asher's logical but perhaps over-simplified approach to the problem (December 9, p. 1564), reflects the widespread confusion of thought which has surrounded this subject ever since the Medical Research Council published its premature condemnation of the use of corticosteroids in chronic asthma five years ago.[1] It must now be patently obvious to every physician with experience in the treatment of asthma, except apparently to Dr. Peter Elmes (November 11, p. 1290), that corticosteroid therapy can be of the greatest value in chronic asthma, and that in many cases it is the only effective treatment available. Every attempt should, of course, be made to avoid giving corticosteroids continuously, and some patients can indeed be kept well by occasional short courses of treatment. These are, however, the exception, and most patients with true chronic asthma relapse so quickly when corticosteroids are withdrawn that continuous treatment is often the only alternative to a life of seriously restricted physical activity. Difficulty in "weaning" such patients from corticosteroid therapy is inevitable, as one is treating a chronic disease with an agent which suppresses its manifestations but does not cure it. Those who withhold continuous treatment from patients who need it and who seem likely to benefit from it, simply because "weaning" may be difficult, are ignoring the natural history of chronic asthma and the mode of action of corticosteroids.

The implication made by the opponents of continuous corticosteroid therapy that effective alternative treatment is available for severe cases of chronic asthma is to my mind quite unrealistic. The medical profession in general has a very healthy respect for the dangers of prolonged corticosteroid therapy, and it is difficult to believe that any responsible doctor would advocate it without first giving simpler measures a fair trial. The root of the matter is that many people are so obsessed with the risks of corticosteroid therapy that they completely underestimate the misery and danger of unrelieved chronic asthma. This is particularly true of chronic asthma in childhood. There is no real evidence to show that prolonged corticosteroid therapy is any more dangerous to children than it is to adults. On the other hand, severe chronic asthma in a child can produce a gross pigeon-chest deformity and permanent pulmonary damage, which can often be prevented by timely treatment with corticosteroids. A pigeon-chest deformity can even be corrected if treatment is started soon enough.

Unfortunately, some patients with chronic asthma when given corticosteroids experience a feeling of wellbeing without showing any objective improvement in ventilatory capacity. If these patients are given prolonged treatment a form of addiction seems to develop and they eventually reach the stage of being unable to do without corticosteroids while deriving no real benefit from the treatment as far as their respiratory symptoms are concerned. Such patients are being needlessly exposed to the danger of side-effects from drugs which have no specific effect on their asthma. Therapeutic mismanagement of this kind could be avoided if the response to corticosteroids of every candidate for continuous treatment were first assessed objectively by ventilatory-function tests.

Finally, might I point out that in many cases chronic asthma can be controlled by giving corticosteroids intermittently, e.g., prednisolone, 20 mg. per day on three consecutive days per week, or 17.5 mg. per day on two consecutive days in every four? In the Respiratory Diseases Units of the Northern General and City Hospitals in Edinburgh we have been using these therapeutic regimes for the past seven years, and an account of the results we have obtained will be published shortly. Although complete control of asthmatic symptoms is not always attainable with these regimes, most patients achieve and maintain a sufficient measure of improvement to allow them to lead active and useful lives. The great advantage of giving corticosteroids intermittently in one of these ways is that serious side-effects are never produced. With continuous daily treatment, which a few patients seem to need, side-effects of greater or lesser severity are bound to develop in a proportion of cases. Even with this form of treatment, however, catastrophic side-effects are not common, and I have personally no doubt that the benefits of well-managed corticosteroid therapy far outweigh the risks involved.—I am, etc.,

I. W. B. GRANT.

Chest Unit,
City Hospital,
Edinburgh 10.

REFERENCE

[1] *Lancet*, 1956, **2**, 798.

SIR,—After reading Dr. J. P. Knowles's article entitled "Difficulties in Weaning in Steroid Treatment of Asthma" (November 25, p. 1396) I am at some loss in assessing the value of his contribution.

It would seem from his conclusions that those cases receiving no benefit from steroid therapy could be weaned from treatment, that those requiring therapy for intermittent attacks should only be treated intermittently, and that those patients who appear to benefit could only be weaned at all with difficulty. One case which died while on steroids is recorded, but the significance of this is doubtful and statistically unimportant. No mention of any serious side-effects when continuous therapy is given can be found. The two or three cases in group D in which treatment was stopped would accord with general experience, though the dosage in these cases is not recorded.

I feel there is an important place for steroid therapy in certain cases of asthma. The value of this treatment can only be assessed in the individual case by the practitioner who is called upon in the first instance maintaining a highly critical state of mind, when he compares the state of his patient as known to him before steroid therapy with that while receiving it. In my view this initial treatment should never be with cortisone but with one of the newer steroids and should not exceed, except in desperate cases, the "cortisone equivalent" of 100 mg. daily—not the high doses elsewhere recorded.—I am, etc.,

Brighton, Sussex. S. L. KAYE.

Recurrent Abdominal Pain in Children

SIR,—The monograph by Apley[1] reports the only long-term follow-up of children with recurrent abdominal pain. He found that of 30 children who had this symptom, 21 had symptoms at the follow-up eight to twenty years later. Twelve of the 30 were suffering from abdominal pain, usually with other symptoms. As Drs. R. H. Jackson and A. R. Bird (November 25, p. 1399) quote from this monograph, it is a pity they have not produced comparable evidence to support their assertion that "recurrent abdominal pain in children . . . usually proceeds to a spontaneous cure." Such attacks of abdominal pain may temporarily cease or shift to a different organ, but a realization of the true outlook would encourage more vigorous pursuit of correct diagnosis and rational treatment, which, as Apley has suggested, will usually be of a psychological disharmony.—I am, etc.,

Guy's Hospital, London S.E.1. R. C. MAC KEITH.

REFERENCE

[1] Apley, J., *The Child with Abdominal Pains*, 1959. Blackwell, Oxford.

Meckel's Diverticulum

SIR,—I read with interest the article on Meckel's diverticulum in childhood by Dr. R. H. Jackson and Dr. A. R. Bird (November 25, p. 1399).

Recently I saw a man of 25 years who complained of abdominal pain felt in the right iliac fossa and the right hypochondrium and sometimes in the epigastrium, radiating through to the back. There was a five months' history. On questioning, he admitted to what sounded like melaena on one occasion. The thing that struck me about the history was that it would have done fairly well for a history of a peptic ulcer case but that food did not relieve the pain. Examination was entirely negative.

He had had a barium meal and a cholecystogram with negative results elsewhere. I took him to see Mr. David Levi at the Uxbridge Cottage Hospital and he recommended an intravenous pyelogram, a Hb estimation, and a blood count. He was good enough to humour me when I suggested that the patient was probably a case of Meckel's diverticulum, and he asked that he might be admitted for appendicectomy and to see whether he might have a Meckel's diverticulum. His Hb was 106%, W.B.C. 6,500 per c.mm., and the blood film was normal. *X*-ray of lumbar spine and intravenous pyelogram were normal.

At operation an appendix which appeared normal was removed. A Meckel's diverticulum was also found and removed, and its presence was acknowledged very handsomely by Mr. Levi.

The pathological report was "Meckel's diverticulum lined by small intestinal type mucosa. No ectopic tissues seen. No gross histological abnormality of appendix."

The patient's mother is a nursing sister in a factory of which I am medical officer. She states that the patient vomited feeds for the first six months of his life, and that throughout his childhood he had bouts of abdominal pain. She saw him in the last six months in bouts of pain which she was convinced were not functional.

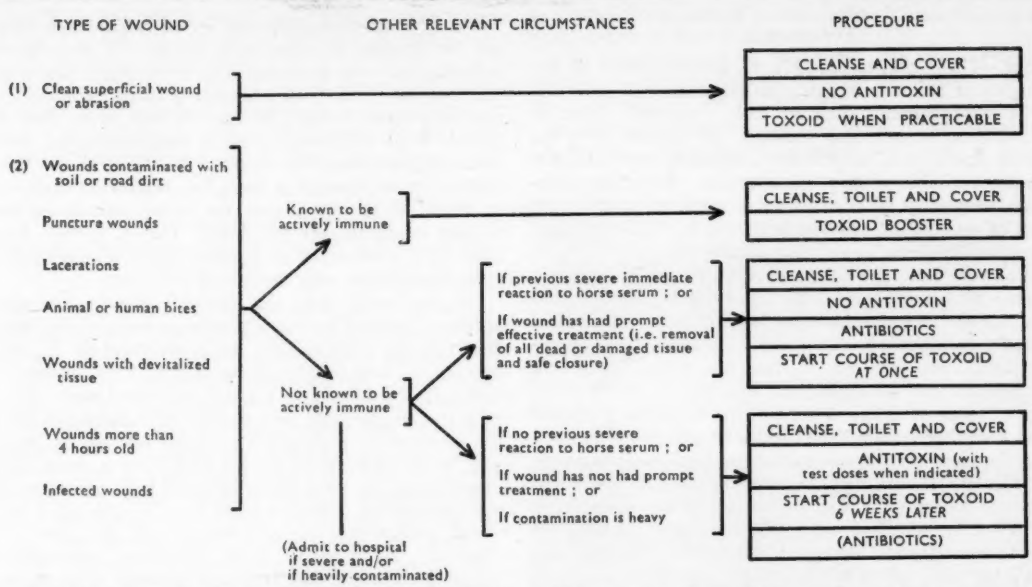
Now we must wait to see whether he casts doubt on the summing-up of Drs. Jackson and Bird—are his symptoms at an end, and therefore is laparotomy justified in children with recurrent abdominal pains unassociated with haemorrhage or obstruction, in the hope of finding a Meckel's diverticulum? And is it justifiable to perform laparotomy in adults with a peptic ulcer-like history but with pain unrelieved by antacids or food, in the hope of finding a Meckel's diverticulum?—I am, etc.,

Eastcote, Middlesex. T. DAVID LAMBERT.

Antitetanus Immunization

SIR,—The prophylactic use of tetanus antiserum in patients with open wounds has fallen under a cloud because of the risks of severe reaction and, in those previously inoculated with horse serum, of inadequate protection. It is tempting to escape from the dilemma simply by using toxoid instead of antiserum for routine prophylaxis, as advocated by Dr. G. E. Fulford and by Dr. Pincus Catzel (November 25, p. 1434). But since, as Dr. Fulford points out, most people have not been actively immunized, a single dose of toxoid at the time of injury will usually have no prophylactic value; even if it is made the first dose in a course of active immunization, its usefulness in that respect will have no bearing on the risk of tetanus which the patient runs in respect of his present injury.

Keeping the whole population in a state of active immunity is the obvious long-term solution to this dilemma; but for those who on injury cannot at present be safely or adequately protected either by antiserum or by a dose of toxoid, antibiotics are surely an important and neglected third means of prophylaxis. By inhibiting the growth of *Clostridium tetani* and, in consequence, the production of toxin, prompt systemic treatment with penicillin, erythromycin, or the tetracyclines has been reported to prevent the development of tetanus in animals inoculated with spores of *Cl. tetani*[1 2 3]; tetanus bacilli were apparently destroyed after a short course of treatment with a tetracycline.[1] It would be useful to have evidence of the protective value of antibiotics in man comparable with that which was obtained in the first and second world wars respectively for antiserum and for toxoid; the studies on animals, however, give reason for regarding antibiotics as possibly more effective prophylactic agents than antiserum,[1 2] and injured persons who cannot be protected


TYPE OF WOUND
OTHER RELEVANT CIRCUMSTANCES
PROCEDURE
(1) Clean superficial wound or abrasion
CLEANSE AND COVER
NO ANTITOXIN
TOXOID WHEN PRACTICABLE
(2) Wounds contaminated with soil or road dirt
Puncture wounds
Lacerations
Animal or human bites
Wounds with devitalized tissue
Wounds more than 4 hours old
Infected wounds
Known to be actively immune
CLEANSE, TOILET AND COVER
TOXOID BOOSTER
Not known to be actively immune
If previous severe immediate reaction to horse serum ; or
If wound has had prompt effective treatment (i.e. removal of all dead or damaged tissue and safe closure)
CLEANSE, TOILET AND COVER
NO ANTITOXIN
ANTIBIOTICS
START COURSE OF TOXOID AT ONCE
If no previous severe reaction to horse serum ; or
If wound has not had prompt treatment ; or
If contamination is heavy
CLEANSE, TOILET AND COVER
ANTITOXIN (with test doses when indicated)
START COURSE OF TOXOID 6 WEEKS LATER
(ANTIBIOTICS)
(Admit to hospital if severe and/or if heavily contaminated)

by serological methods should certainly not be deprived of antibiotic protection when prophylaxis seems desirable.

Selection of the appropriate antibiotic (or antibiotics) presents some difficulties. For most patients penicillin, preferably combined with a sulphonamide to inhibit penicillinase-producing organisms, would be practical and appropriate, but oxytetracycline or erythromycin are probably more appropriate for severely injured patients in hospital. The following Chart shows how antibiotic prophylaxis might be integrated with the other available measures of prophylaxis against tetanus.—We are, etc.,

E. J. L. LOWBURY.
R. L. BATTEN.
P. S. LONDON.

Birmingham 15.

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1 Anwar, A. A., and Turner, T. B., *Bull. Johns Hopk. Hosp.*, 1956, **98**, 85.
2 McDonald, R. T., Chaikof, L., and Truant, J. P., *Surg. Gynec. Obstet.*, 1960, **110**, 702.
3 Taylor, W. I., and Novak, M. V., *Ann. Surg.*, 1951, **133**, 44

Multiple Sclerosis and Cancer

SIR,—Recent publicity in the lay press prompts this letter, first to disavow any connexion of this Group with the proposed therapeutic experiment of transfusing serum from patients with multiple sclerosis into patients with advanced cancer (*The People*, December 3), and second to make some general observations on the subject.

Affinities and antipathies between various diseases have long excited interest, and no doubt validated observations on these lines must ultimately be incorporated into any broad system of aetiological pathology. Unfortunately, they are few and far between. The suggestion of a dissociation between cancer and multiple sclerosis is not a new one. Schaltenbrand[1] in 1957 stated that cancer was seven times less frequent in multiple sclerotic cases than in a comparable cross-section of the general population: it should be noted that these observations were based mainly on necropsy material and although highly suggestive they cannot be applied without reservations which could only be overcome by careful and protracted population studies. In the same paper Schaltenbrand records the relative infrequency of diabetes in multiple sclerosis, and other writers have suggested a decreased incidence both of atherosclerosis and hypertension.

It would be, to say the least, a long shot to undertake the treatment of hypertension or diabetes with multiple sclerosis serum; but very long shots do occasionally come off, and we can only wish every success to our colleagues whose prospective plan of treatment has been so phrenetically publicized. Since the infective hypothesis of multiple sclerosis has not yet been completely discounted, we hope that the nervous systems of patients so transfused will be subject to meticulous histological examination.—We are, etc.,

Medical Research Council Group on Demyelinating Diseases, Newcastle upon Tyne 2.

E. J. FIELD.
HENRY MILLER.

REFERENCE

1 Schaltenbrand, G., in *Premier Congrès International des Sciences Neurologiques, Bruxelles, 1957, 3e Congrès International de Neuropathologie*, 1957. Rapports et Discussions, p. 85. Éditions Acta Medica Belgica, Brussels.

Personal Medical Records

SIR,—In their letter (December 16, p. 1647) on personal medical records, Drs. John Fry, H. J. Parish and D. A. Cannon reiterate an objection that has often been made to a single tattoo mark—namely, that it gives no indication of the date of active immunization against tetanus or of reinforcing injections. This objection ought not to be taken too seriously. Regamey and Schlegel[1] found that persons who had three primary doses of tetanus toxoid responded readily to a reinforcing dose 10 years later. For practical purposes, therefore, all a casualty officer needs to know is that the wounded child has been primarily immunized against tetanus, and may therefore be expected to respond to a fresh dose of tetanus toxoid.—I am, etc.,

Public Health Laboratory Service Board, London W.1.

G. S. WILSON.

REFERENCE

1 Regamey, R. H., and Schlegel, J. J., *Z. allg. Path.*, 1951, **14**, 550.

"Nervessa"

SIR,—I was glad to read Dr. K. Lancer's letter on the dangers of bromide intoxication (December 9, p. 1571). It is not generally realized how frequently bromide intoxication occurs, and addiction to bromide is by no means uncommon, as bromide-containing hypnotics are readily available without prescription. Other bromide-containing drugs have also been a cause of trouble, and I have one patient who is addicted to "Gabail elixir bromo-valerianate."

Not very long ago I had referred to me an epileptic whose medication had been changed by her general practitioner to bromides; she was confused, orally and visually hallucinated, and quite unmanageable at home. Her condition rapidly cleared up when alternative medication was arranged.

A number of drugs in general use for other purposes than sedation contain bromides or organically combined bromine, and these too can give rise to chronic bromide intoxication surprisingly quickly in elderly or arterio-sclerotic patients. I am sure that, if the dangers of bromide intoxication were more widely understood, much less bromide would be dispensed. I would also like to see bromide-containing preparations made subject to the Dangerous Drugs regulations. I entirely agree with Dr. Lancer that the profession must strongly condemn the unrestricted sale of "nerve tonics" containing bromides.—I am, etc.,

Fairdene and Netherne Hospitals, Coulsdon, Surrey. H. E. S. MARSHALL.

Trends in Child Psychiatry

SIR,—While your admirable leading article (December 9, p. 1551) puts into perspective the letter from Professor Desmond Curran and Dr. Gerald Garmany (December 2, p. 1500), there remain other points in that letter which should not go without comment.

The most obvious of these is the plea for the discarding of the term "child guidance." In its original concept the term was to be taken literally. It assumed that before a child became notably maladjusted he passed through a phase during which psychiatric treatment as such was not indicated; in that phase it might be possible to avert or minimize emotional troubles by "guiding" the family or the school in their management of the child or by helping the child himself to understand his problems. This would be more of a social and educational task than a psychiatric one.

I have seen no evidence that this concept is intrinsically invalid and the use in the letter of the phrase "We have not seen many instances where 'guidance' in any way covered the work that was done" implies that some such cases have been seen. If they are few in number, there are several possible explanations. One is that this anticipatory work is being done by child welfare and school medical officers with the help of educational psychologists, teachers, and the staff of the local authority child health services. In some degree this is true, but school medical officers themselves would be the first to admit that many of their number still need to know more about child psychology and psychiatry and that they like to have easy access to psychiatric advice.

A second reason might be that "guidance" is not often successful. This would be difficult to demonstrate; in all fields of medicine statistics of illness prevented are hard to come by, and children who had been "saved" from maladjustment by early guidance would not be brought to psychiatric clinics. It is, however, possible and even probable that emotionally vulnerable children are not being detected early enough for guidance alone to be effective. If that is so, then the answer is not for psychiatrists to wait in hospital clinics until maladjustment has reached the point at which the child must be brought to them for treatment; they must be ready to go out to seek the vulnerables or at least to help others to seek for them. This is, in fact, being tried by a number of progressive child psychiatrists in close association with child welfare clinics.

No one would deny that the child psychiatrist needs access to hospital facilities, general as well as psychiatric, and that he should have an understanding of adult psychology and psychiatry so that he may understand and help the family as a socio-emotional unit. But if he is to give the right help early and to make full use of the therapeutic potentialities of the schools—a matter well worth consideration—he must have a more direct contact with the local authority child health services and the educational administration than is possible if he is based exclusively on a hospital. If the quest for "health" is to mean more than the treatment of established illness, then the mental health services must have outposts in the community and not merely fortresses in the hospitals. The child guidance clinic is precisely such an outpost. It may, and probably does, need improvement and the present time is a good one to look at it critically. But to abandon it would be crass defeatism.—I am, etc.,

Public Health Department, Colchester. JOHN D. KERSHAW.

SIR,—The memorandum of the Association of Teachers of Psychiatry in Undergraduate Medical Schools (December 2, p. 1500) has a disarming old-world ring about it, but it ignores at least some of the most important trends in this and other countries. Heaven knows that there is great need for the improvement of the teaching of child psychiatry to medical students and of the treatment of psychotic children. It may well be a pity that some child guidance clinics have educational psychologists as directors now that a growing number of children under school age and a few who have already left school attend, but we would appreciate that, when these clinics were conceived, there were too few child psychiatrists to staff them and it was the educational authorities and not the hospitals that took the lead in their establishment.

The great need now is for the development of preventive services, and child guidance clinics in the community are ideally disposed to do this as a complement to the child psychiatric clinics in the hospitals. As Caplan[1] has recently written, "The treatment of individual sick children can never provide an adequate solution to the problem of mental disorder among a population of children." The child guidance clinics are in a position, if they have the will, to work to this end with the key people in the community, teachers, social workers, and magistrates as well as health visitors, midwives, nurses, and doctors, and if despite their waiting-lists these clinics were removed it would be necessary to re-create them to try to do this.

As for that Aunt Sally the Care Committees of London, they were, it is true, associated with the opening of the first clinic in England, but now their "dominant role" is only that of knowing which clinic

in any area has the shortest waiting-list. Less than half the London schoolchildren referred to clinics are sent via the Care Committees.

This is hardly a time to relight old fires—both local authorities and hospitals have their contributions to make, and the circulars of the Ministries of Health and Education were written to emphasize the common aim of both.—I am, etc.,

Hassocks, Sussex. DENIS PIRRIE.

REFERENCE

[1] Caplan, G., *Prevention of Mental Disorders in Children*, 1961. Tavistock Publications, London.

SIR,—I must draw attention to an apparent misrepresentation of the views of undergraduate teachers of psychiatry which appeared in your issue of December 2 (p. 1500). As originally presented to the general meeting of the Association of Undergraduate Teachers of Psychiatry the memorandum you printed contained a statement to the effect that the best site for a child guidance clinic is a paediatric hospital. This view was challenged by many members present; amongst other reasons because a very critical period for children is puberty, because the child psychiatric service needs to be integrated with the developing service for adolescents and because the psychiatric treatment of children sometimes requires adequate facilities for the psychiatric treatment of adults. It was agreed that this recommendation should be changed to the sense that child psychiatric clinics could best be sited "either in a paediatric hospital or in a general hospital *with* a paediatric department," not "in a general hospital *within* a paediatric department."—I am, etc.,

London N.W.3. ALICK ELITHORN.

Industrial-bullet Wound

SIR,—This is an account of an injury from a threaded pin, fired from a cartridge-operated tool which is nowadays widely used in the building trade (Fig. 1). A variety of metal pins can be driven into steel or concrete for the purpose of attaching other structures. The driving force required is provided by the explosion of a .22- (or 10 mm.-) calibre cartridge. When loaded with cartridge and pin, the tool is pressed firmly against the surface into which the pin is to be fixed. It is only in this position and on exerting the pressure that detonation of the cartridge will occur on pulling the trigger. Certain other safety features are incorporated in the design of the tool, and the manufacturers provide instruction in its use for workmen on building sites.

As there is still a potential danger if the tool is improperly handled, it is essential that the manufacturers' explicit warnings and safety measures are closely followed, and that workmen are fully instructed in the handling of the tool by the manufacturers' representative.

A workman from a near-by building site was admitted to hospital with a gunshot injury in the region of his left shoulder. On examination he was pale and looked shocked. His pulse rate on admission was 90 per minute and blood-pressure 170/80. An entrance wound was present at the level of his left nipple in the anterior axillary line. A hard lump was palpable in the soft tissues above his left supra-scapular fossa. There was no evidence of any motor or sensory impairment in his left upper limb. Brachial and radial pulses were palpable. A radiograph of his left shoulder showed a fracture at the junction of the middle and outer thirds of his clavicle, and a film of the cervical spine (Fig. 2) showed the position of the "bullet." A chest *x*-ray was normal.

After blood transfusion, the missile was removed under general anaesthesia through a small transverse incision above the spine of his left scapula.

Subsequently the patient has made good progress. Three months after injury his left clavicle was clinically

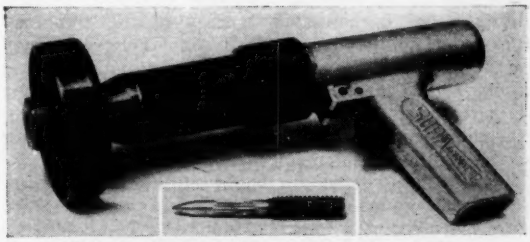


FIG. 1.—The cartridge-operated tool, and pin.

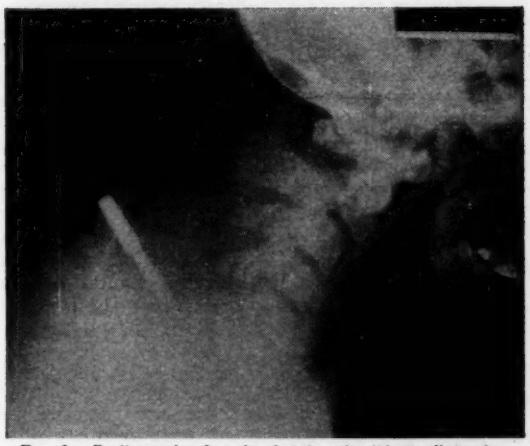


FIG. 2.—Radiograph of neck, showing the "bullet" *in situ*.

united. He had a full range of active movements in his left shoulder and he was fit to return to work.

I would like to thank Mr. A. Cameron MacLeod for permission to record this case, Professor A. J. Harding Rains for his encouragement, and the manufacturers, F. H. Bourner (Fixings) Ltd., Crawley, Sussex, for their generous information.

—I am, etc.,

Charing Cross Hospital, London W.C.2. L. KLENERMAN.

Psychomotor Epilepsy

SIR,—The first Goulstonian Lecture by Dr. D. A. Pond (November 25, p. 1377) and Liddell and Margerison's[1] recent work raise a problem to which I may have previously pointed the solution.[2] If the psychomotor area of the cortex consists of adjoining parts of the paracentral lobule and the precentral and frontal gyri, then why do electroencephalographic spikes in patients with psychomotor epilepsy occur in the temporal lobe?

All movement has admittedly motor and sensory features, but, as will be enlarged upon below, the relationship in this instance is far from simple. In motor learning we are not aware of the motor elements or proprioceptive impulses, most of which do not reach our consciousness, so much as the exteroceptive changes —for example, of touch—on the skin of the limb being

moved, or the visual pattern it may make as it passes through the environment. The problem as to how we will ourselves to make a voluntary movement when motor elements do not enter consciousness presents difficulties in this arrangement, but I believe that may be part of the much greater one of motivation in general on which I have enlarged elsewhere.[3] If, however, motor learning does thus consist of facilitation related to conscious sensory guides, this may provide a solution to the problem. Dyspraxia may arise from lesions of the sensory association cortex (lying behind the central sulcus), and the temporal lobe is part of this area, so that epileptic discharges, being the equivalent of stimulation rather than ablation, might result in automatism, much as stimulation of the sensory side of a simple reflex arc would result in action.

Fibre connexions between sensory and motor (pre-central) cortex have yet to be clearly established, however, especially since the superior longitudinal fasciculus, for example, a previously accepted connexion, appears now to turn medially into the caudate nucleus as it passes backwards from the prefrontal region and not outwards to the cortex.[4] It seems likely, therefore, that the relation between sensory and motor function in the cortex and the nature of psychomotor epilepsy is more subtle than one simply dependent upon directly associating tracts. Since adroit distribution of attention is now an accepted major function of the prefrontal areas, I have suggested that by directing the sensory organs of attention, and in man in particular the eyes, the motor cortex may co-ordinate itself indirectly with its sensory counterpart, possibly through the striato-cortical mechanism discussed by Mettler.[5]—I am, etc.,

Ide Hill, Kent. J. P. CRAWFORD.

REFERENCES

[1] Margerison, J. H., and Liddell, D. W., *J. ment. Sci.*, 1961, **107**, 909.
[2] Crawford, J. P., *Excerpta med. (Amst.) Sect. VIII*, 1957, **10**, No. 5103.
[3] —— *Med. Press*, 1960, **244**, 525.
[4] Beck, E., 1957, personal communication.
[5] Mettler, F. A., *Psychiat. Quart.*, 1955, **29**, 89.

Amputation Through the Knee

SIR,—In replying to the letters of both Mr. Peter Martin (December 2, p. 1495) and Mr. Roland N. Jones (p. 1496), I would like to say that I am in agreement with much of what they have said.

Although the Stokes–Gritti amputation, successful from the surgical point of view, was originally designed to give an end-bearing stump, I think most surgeons will agree with Mr. Peter Martin that it has not proved to do so. A successful through-knee amputation, however, *is* end-bearing. Moreover, as the condyles have their normal expanded shape, the end of the stump is broader than the thigh; this helps to retain the thigh-piece of the artificial limb, and hence to diminish the pull from waist-belt or shoulder-suspension. In comparison, the stump resulting from a Stokes–Gritti amputation (the shaft of the femur being divided at a point before it expands to the condyles) is conical, and has no retaining power: all the weight of the artificial limb must be taken from the belt or from the shoulder harness.

Of course, a through-knee amputation cannot be carried out if there is insufficient viable skin for the flaps, but in my experience there are a number of patients with arteriosclerosis of a degree sufficient to preclude a below-knee amputation but with sufficient blood supply through the geniculate anastomosis to maintain the necessary skin flaps of the through-knee amputation. If there is insufficient viable skin to permit a through-knee amputation, one should consider carefully whether the extra 2–3 in. (5.1–7.6 cm.) of the Stokes–Gritti stump does in practice offer any real worthwhile surgical advantage over the shorter standard above-knee stump. From the prosthetic point of view it is my opinion that the advantage (such as it is) is illusory, for there is no doubt that the type of limb to which a Stokes–Gritti amputee is restricted is a functionally less efficient prosthesis than that with which a standard above-knee amputee can be fitted. Again, should the patient be unfortunate enough to lose his second leg, he is very much more comfortable and more mobile with two through-knee amputations than with two Stokes–Gritti amputations.

Mr. Roland Jones has drawn attention to the time taken in the manufacture of a permanent pylon or an artificial limb. This is fully realized and deplored by the limb-fitting service, but it should be remembered that a comprehensive service of this magnitude is dependent not only on doctors, whose desire to help patients is undoubted, but by manufacturers who in turn are dependent on expert labour. One has merely to scan the daily newspapers to realize the difficulty that is experienced to-day in industry.

I would therefore reiterate my praise for this comprehensive service and its ability to deal with amputation stumps of all types, including the Stokes–Gritti. But I believe that, unless a particular amputation confers some proven benefit on the patient either surgically or prosthetically, it is logical to replace it by another.—I am, etc.,

Queen Mary's Hospital, Roehampton, London S.W.15. LEON GILLIS.

Economical Use of Nursing Ability

SIR,—May I congratulate Dr. W. Ritchie Russell on his letter (December 9, p. 1569)? Having practised for over 30 years within a few miles of the teaching hospital where he is on the consultant staff, I can endorse every word he says.

Might I go further and suggest that the clever women who run the General Nursing Council and Royal College of Nursing should take a spell off and do some real ward nursing for a change, or alternatively arrange to be admitted to hospital themselves and be looked after by nurses trained very largely in the lecture theatre?—I am, etc.,

Stoke Abbott, Beaminster. D. A. BRIGG.

Free Beer

SIR,—The art of preparation of food and drink is not to be despised. Art, as Tolstoy said, is a means of conveying emotion between individuals, and thereby helps man to fight one of his arch-enemies, loneliness. In its own way the beer, of which we have recently been given a free sample, deserves the highest praise as a work of art. Nevertheless, I doubt whether a doctor, save in exceptional circumstances, is wise to prescribe alcohol in any shape or form. It is a drug of addiction, it is a gastric irritant, and it reduces skill in the handling of machines, notably motor vehicles, and a doctor's words normally carry much weight.—I am, etc.,

Barton-on-Humber, Lincs. S. H. F. HOWARD.

Obituary

Sir EARLE PAGE, P.C., G.C.M.G., C.H., Hon.D.Sc. M.B., Ch.M., Hon.F.R.C.S., F.R.A.C.S.

The Right Honourable Sir Earle Page, one of the most colourful personalities in Australian politics, died in Sydney on December 20. Before he gave up medicine for public life he had built up a large medical and surgical practice in the north of New South Wales. He was Deputy Prime Minister of the Commonwealth of Australia in two Governments, and for a short time in 1939 was Prime Minister. He held many other Government posts and under Mr. Menzies was Minister of Health when Australia introduced a national health service. Describing the scheme at the General Assembly of the World Medical Association in 1953, Sir Earle said:

"The Australian Government believes . . . that a partnership of the medical profession, the community, insurance companies, and the Government can evolve a method of retaining all the existing traditions and advances on the medical side and still bring the cost of a first-rate medical service within the means of the people."

[*Universal Pictorial*

Sir Earle Page retired from the Australian Cabinet in 1955, but he lived an energetic life until very recently. He was 81 when he died.

Earle Christmas Grafton Page was born on August 8, 1880, the fourth son of Mr. Charles Page, a coach builder of Grafton, New South Wales. He was educated at Sydney High School and at the University of Sydney, graduating M.B., Ch.M. in 1902. He had had a distinguished student career, winning scholarships in anatomy, physiology, and mathematics, and being placed first in his year in his final examinations. After graduation he held the appointment of resident medical officer at the Royal Prince Alfred Hospital, Sydney, and then went into practice at South Grafton, where he quickly made a name for himself as a physician and surgeon over an area 200 miles long and 80 miles wide. He established his own hospital at Grafton. Early in his career he became interested in public works and pioneered the Nymboida electricity scheme.

In 1916 he enlisted in the Australian Imperial Forces for service in the first world war, during which at various times he was senior medical officer in H.M.A.S. *Ballarat*, surgeon to the 3rd Australian General Hospital in Egypt, and surgical specialist to No. 3 Australian casualty clearing station in France. In 1927 he was elected a Foundation Fellow of the Royal Australasian College of Surgeons.

Earle Page became mayor of Grafton in 1918, and in the following year he was elected to the Federal Parliament as the representative for Cowper, New South Wales. He was the leader of the Australian Country Party from 1920 to 1939, and Commonwealth Treasurer from 1923 to 1929. Over a period of more than thirty years he held many high offices in the Government, being acting Prime Minister in 1923–4, 1926–7, 1935, and 1937; Deputy Prime Minister and Minister of Commerce from 1934 to 1939; Minister for Health in 1937–8 and again from 1949 to 1956; Prime Minister in 1939; and Minister of Commerce again in 1940–1. He was a member of the Australian War Cabinet in 1942–3, and of the Australian Advisory War Council from 1942 to 1945. He made several visits to England. During the second world war, in 1941, he was appointed by his Government to come to London to establish personal liaison between the United Kingdom Government and that of the Commonwealth. In 1942 the Prime Minister of Australia arranged that Page would attend the meetings of the War Cabinet in London, so that the knowledge and experience he gained as representative of Australia in the United Kingdom War Cabinet and on the Pacific War Council would be available to the Commonwealth Government. Having been made a Privy Councillor in 1929 he was appointed G.C.M.G. in 1938 and admitted to the select company of Companions of Honour in 1942.

While Sir Earle Page was representing his Government in London in 1942 the Royal College of Surgeons of England conferred on him the Honorary Fellowship of the College. The President, Sir Alfred Webb-Johnson, as he then was, said at the ceremony that Sir Earle's colleagues had watched with interest and pride his political career but had not forgotten his services to surgery. In reply Sir Earle remarked that a surgical training was invaluable in the political field because what was so much needed there, and so seldom took place, was diagnosis before treatment. He believed that with the combination of diagnosis before treatment, quick decision, and immediate action many of the national and probably all the international ills would never arise at all.

Earle Page was the first chairman of the Australian Agricultural Council. When the New England University was established in 1955 he was elected its first Chancellor, and at his installation the ceremony began with the conferment on him of the university's first honorary degree of D.Sc. In acknowledging the honour he said, "No honours I have gained have inspired me as this has done, nor given me the same sense of personal pride and pleasure." Three years earlier the University of Sydney conferred on him a similar honorary degree.

Apart from his political and professional life he had been an active and successful farmer on a large scale, opening up important new dairy farming areas. He was an acknowledged authority on water conservation, irrigation, and electricity, and was the author of several works on these subjects.

Sir Earle Page met his first wife, Miss Ethel Blunt, when she was a nurse at the Prince Alfred Hospital, Sydney. She died in 1958, and in 1959 he married Miss Jean Thomas, who survives him. By his first marriage he had three sons and a daughter. He had the misfortune to lose two of his sons, one being killed by lightning and another drowned in a flooded river.

G. S. HAYNES, M.D., F.R.C.P.

The death of Dr. George Haynes on December 9, at the age of 89, removes another of the dwindling number of those who were privileged to practise before the introduction of the National Insurance Act of 1911. He was formerly honorary physician at Addenbrooke's Hospital, Cambridge.

George Secretan Haynes was born on July 15, 1872, and went on to St. Bartholomew's Hospital for his clinical training after leaving Cambridge. He qualified in 1897 and following a resident post at the Belgrave Hospital for Children he returned to Cambridge as house-physician at Addenbrooke's Hospital and remained to practise there for the rest of his life. He graduated M.B., B.Chir. in 1903, and proceeded M.D. in 1907, having been admitted to King's College. After a period in general practice he was appointed consultant physician to Addenbrooke's Hospital in 1920 and became widely known throughout East Anglia. He took the M.R.C.P. in 1920 and was elected F.R.C.P. in 1932.

R. E. writes: Those of us who knew him well remember Dr. George Haynes's geniality and kindness. In consultation he was painstaking and sound in his judgment. Over

such a long period he was naturally called upon to hold many offices in connexion with his profession. He was honorary secretary of the Cambridge and Huntingdon Branch of the B.M.A. from 1920 to 1929, and he was president of the Branch in 1938–9: I recall the kindly manner in which he installed me as his successor in this office in 1939. At the B.M.A. Annual Meeting in 1920 held at Cambridge he was honorary local secretary. In the following year at Newcastle upon Tyne he was vice-president of the Section of Medicine. He also took his turn as president of the Cambridge Medical Society.

On his retirement under the age rule as physician at Addenbrooke's Hospital, he became chairman of the National Service Medical Board which was set up in June, 1939, at Cambridge to examine the so-called Militia—I remember with pleasure attending the first session of the board with him: although we did not know it then, the Board was to last 20 years. During half this time George Haynes was chairman, and his unruffled genial disposition suited him admirably for the task. He made his team and the Service men who came up for examination feel at ease and contented. Those of his contemporaries who still remain will wish to sympathize with his son and two daughters who survive him.

M. B. LAVERY, M.B., B.Ch., M.Sc., F.R.C.S. F.R.C.S.Ed.

Mr. Maurice Lavery, senior surgeon at Belfast City Hospital and consultant surgeon to the Mater Infirmorum Hospital, died on December 9 at the age of 60.

Maurice Basil Lavery was born in Belfast and educated at the Irish Christian Brothers' School and Queen's University, where he had a distinguished career, graduating B.Sc. in 1922 and M.Sc. in anatomy (with honours) and M.B., B.Ch. in 1925. After holding the post of demonstrator in anatomy at Queen's University he obtained his higher surgical qualifications—the Fellowship of the Royal Colleges of England and Edinburgh—while a registrar in surgery at Sheffield Royal Infirmary.

Returning to his native city, he was appointed consultant surgeon to the Mater Infirmorum Hospital, a post which he retained until his death after a long and devoted service. Some 20 years ago he was appointed as a consultant surgeon to the Belfast City Hospital, and for many years also he occupied the post of lecturer in operative surgery in Queen's University. Though skilful in all aspects of general surgery, his special leaning was towards abdominal surgery, in which he excelled. No operation was undertaken without a great deal of time and thought being spent in its consideration and infinite care and attention in its after-treatment. His careful dissection and gentleness with the tissues were features of his early anatomical training and characterized his work.

Those who knew him well, knew him as one who above all else in his profession and character was wholly sincere. Whether in matters medical or otherwise his opinions were formed only after most careful deliberation and given with much thought and consideration, and were therefore much valued by his students and colleagues.

Although shy and undemonstrative, he had a deep religious faith allied to an abiding sense of loyalty, and these characteristics may have influenced his decision to give his services unstintingly to the Mater, when he might otherwise have decided to work more comprehensively and lucratively in the National Health Service. While well known as a teacher to succeeding generations of students, he contributed little to medical literature, mainly because of his somewhat sensitive and reserved nature. Nevertheless he imparted to his pupils and house-surgeons the value of his shrewd and painstaking nature, and his impish humour was appreciated by all.

Some months ago his health began to fail, but he was able to continue at work until a week before his death. His intense interest in his work allowed little time for leisure, but fishing was his most absorbing outdoor pastime. As one of those privileged as a student, and later as a registrar, to receive my training from him, may I offer this tribute to his memory, in an attempt to express the sorrow of his friends and colleagues to his devoted widow, who nursed him with unfailing care.—J. P. S.

J. M. M. writes: Mr. Maurice Lavery was essentially an abdominal surgeon with an especial interest in the surgery of the stomach. He was possessed of fine clinical judgment and manual dexterity of a high degree. It was a great experience to assist him at a difficult abdominal operation and to see for oneself with what skill he overcame the problem. He was a great and modest gentleman and will be greatly missed by his colleagues as well as by a vast number of patients, who have reason to thank him for his ability, his care, and his kindness.

A. M. BARRETT, M.D.

Dr. A. M. Barrett, university morbid anatomist and histologist at Cambridge and honorary consulting pathologist to the United Cambridge Hospitals and to the East Anglian Regional Hospital Board, died on December 11, aged 52.

Arthur Max Barrett was born at Thaxted in Essex, where he spent his boyhood. He was educated at Newport Grammar School and at the Cambridge and County High School, where he won a State scholarship in 1927 and a major scholarship to Pembroke College in 1928. His university career was brilliant; he obtained first-class honours in both parts of the Natural Sciences Tripos and was awarded the Shoolbred and Foundress' scholarships. He went to the London Hospital Medical College as an entrance scholar in pathology and won five prizes during his clinical training. He graduated M.B., B.Ch. in 1934 and then worked in the wards and laboratories of the London Hospital until 1938, when he returned to Cambridge as a university demonstrator in pathology. During the war years he was the only demonstrator in the department and shouldered a very large part of the teaching responsibility. Despite this he found time to take an active interest in the routine pathology services of Addenbrooke's Hospital. In 1946 he was appointed to the newly created post of university morbid anatomist and histologist to Addenbrooke's Hospital, continuing in that post until his death. His thesis for the M.D. degree was submitted in 1960 and gained him the Raymond Horton-Smith prize.

His work as a pathologist was always of the highest quality, and his standards were a constant stimulus to all who worked with him. His dissections of the human body were conducted meticulously, skilfully, and systematically; there always remained something to be learned from his conduct of a necropsy. Time became of no consequence on these occasions, and lunch hours flitted by until he was satisfied that no more could be gained from the examination. It was in this way that he often disclosed the unexpected and left his assistants and students with the firm resolve that nothing would be missed next time. At the bench he was a skilled technician, conversant with every aspect of the art of histological technique. He was for many years an examiner for the Institute of Medical and Laboratory Technology, and his advice, patience, and guidance were invaluable to those who examined with him.

He believed in the precise use of language, and this was constantly illustrated in the detailed reports which he made on histological preparations. At the microscope, as in the post-mortem room, he was often able to discover some small but important clue which enabled a firm diagnosis to be made. His advice was constantly sought by pathologists in East Anglia and elsewhere, never without profit. He built up a tradition of the conduct and teaching of morbid anatomy in Cambridge which was of the highest calibre. Unfortunately a great deal of his vast store of knowledge

has died with him, but some of it he communicated by the daily instruction of those who worked with him and by means of clinicopathological meetings which were much appreciated by his clinical colleagues.

As a friend and counsellor he was staunch and always reliable. No decision was taken in haste but only after careful consideration. When he spoke at the Faculty Board of Medicine or as secretary of the Degree Committee everyone recognized it as a carefully balanced statement worthy of consideration.

He enjoyed, among his hobbies, the collection of field fungi. These were carefully preserved, often examined histologically, and recorded with the same care that he gave to all his doings. His family life was a happy one: tea with the Barretts was fun, for he had imparted to his family his unbounded curiosity, which was, in the view of many friends, his most endearing characteristic.

Cambridge and British medicine have lost one who stood in the forefront of pathology. His untimely death is a bitter blow to all who knew him and particularly so to those who worked with him.

To his devoted wife and family we extend our deep condolences, with the small but significant consolation that much of his character lives on with those who had the good fortune to work with him.—G. A. G.

F. M. GREENBAUM, M.D.

Dr. F. M. Greenbaum, who practised as a psychiatrist in Manchester, died in that city on November 1.

Franz Max Greenbaum (he changed his name recently from Grunbaum) qualified at the University of Berlin in 1929. After gaining experience in both general medicine and general surgery, he decided to specialize in psychiatry and proceeded M.D. in 1932. As early as 1926 he had started his own personal analysis with the first Jungian analyst in Berlin, Dr. Sussman, and later completed his training under Jung himself in Zurich. He came as a refugee to Britain in 1939 just before the war, and after war was declared he suffered a short period of internment.

On his release he developed an extensive psychotherapeutic practice in Manchester, and with the introduction of the National Health Service joined the staff of the psychiatric department of Salford Royal Hospital and Hope Hospital. Here, in addition to carrying on both individual and group psychotherapy along Jungian lines, he was not averse to using accepted physical treatments in assisting his patients. In later years he evolved his own method of group therapy, showing a particular ability in using patients' drawings for group analysis.

He handled both neurotic and mixed neurotic and psychotic groups with considerable skill and ability and with excellent results. He was always interested in passing on his knowledge and experience, and just before his health began to fail he ran a study group in Jungian psychology for psychiatrists in the Manchester area, which was very well attended. In addition, he presented numerous papers and seminars in Manchester on his subject.

As an individual he was a man of great charm and complete sincerity, and was possessed of no mean artistic gifts himself. His portraits and caricatures of friends and colleagues would enhance many a pleasant evening shared in his company. He will be greatly missed by all his patients and colleagues and by a wide circle of friends. He is survived by his widow and three daughters.—W. V. W.

THOMAS ROBERTSON, M.B., Ch.B.

Dr. Tom Robertson, physician to the Glasgow Homoeopathic Hospital, died on December 3.

Thomas Robertson was born in Edinburgh in 1894, the son of the Rev. James Robertson. Educated at George Heriot's School, he came to Glasgow in 1911. First attracted by the idea of becoming an engineer, he became apprenticed to the shipbuilding firm of A. & J. Inglis and matriculated at Glasgow University, intending to take a degree in a scientific subject. He switched to medicine, however, graduating B.Sc. (in anatomy and physiology) in 1921 and M.B., B.Ch. (with commendation) in 1923. Before that he had served throughout the first world war in the Royal Navy, having been called up as a member of the R.N.V.R. At the Battle of Jutland in 1916 he was in H.M.S. *Benbow*. After some experience as an assistant in Northumberland and Glasgow, he spent several years in general practice at Strone in Argyll, eventually settling in the West End of Glasgow in 1931.

T. J. H. writes: The death of Dr. Tom Robertson has removed from Glasgow medical circles one of its most colourful characters. He became interested in homoeopathy and was a physician to the Glasgow Homoeopathic Hospital from 1931 to 1960, receiving the M.F.Hom. in 1944. Later he resigned from the National Health Service but continued in private practice until shortly before his death. A tall, kenspeckle, bearded figure, Tom Robertson won the admiration of a great number of people, some of whom were not altogether in sympathy with all his views on a wide range of subjects. There was a streak of genius in the man. As a youth he taught himself to play the violin, reaching a high standard of performance. It could be said of him that his curiosity was insatiable, and it was never superficial. He delved deep into whatever aspect of the art of living had captured his attention—witness his book, *Human Ecology—Science of Social Adjustment*.

He would accept nobody's precepts or instructions if they threatened his own moral or ethical freedom. Regarding his mind as a sacred possession, he could not believe that any rational being could be wrong in doing what he wished to do, if thereby he did not infringe on someone else's rights and privileges.

Throughout his professional life Tom Robertson thought there was a distinction to be made between the physician and the practitioner in medicine. His aim was always to try to be the former. Through his integrity and determination he won the affection and respect of patients and of those who enjoyed his friendship.

He is survived by his wife, his constant companion, and his son, Dr. James Robertson, who is on the staff of the Royal Mental Hospital in Glasgow. A younger brother, J. Fyfe Robertson, is the well-known T.V. personality.

ANDREW CROLL, M.D., F.R.C.S.Ed.
F.R.C.S.(Canada), F.A.C.S.

Mr. Andrew Croll, who for many years was a gynaecologist in Saskatoon, Saskatchewan, died in retirement at Toronto on October 28. He was 90 years of age.

Andrew Croll was born in Dundee, Scotland, on October 8, 1871. Educated at University College, Dundee, and the University of Edinburgh, he graduated M.B., C.M. in 1893 and then studied as a postgraduate in London, Berlin, Vienna, and Budapest. After graduation he practised in Merthyr Tydfil, South Wales, and in Handsworth, Birmingham, where he married. He proceeded M.D. in 1899, and in 1905 he represented his Division at the Annual Meeting of the B.M.A. In 1909 he moved his family to Western Canada, settling in Saskatoon, Saskatchewan, where he was active in setting up Saskatoon's first hospital, St. Paul's, with which he was associated until the time of his retirement. He returned to Edinburgh in 1912 to take the F.R.C.S. In 1914 he was elected F.A.C.S. and in 1931 F.R.C.S. (Canada).

At the outbreak of the first world war, after selecting and organizing the training of a St. John Ambulance group for auxiliary medical services, he went to France as a lieutenant-colonel in the Canadian Army Medical Corps, becoming chief surgeon and officer in charge of surgery at No. 2 Canadian General Hospital at Le Tréport. Returning to

Halifax, Canada, in 1917, he was chief surgeon to Camp Hill Military Hospital and consulting surgeon to the Military District of Nova Scotia.

In 1919 he returned to Saskatoon, where he practised until his retirement in 1947. Apart from an extensive private practice, he was surgical specialist to the Department of Soldiers Civil Re-establishment, Dominion of Canada, the Department of Pensions and National Health, the Department of Veterans' Affairs, and the Canadian National and Canadian Pacific Railways. He was examiner in anatomy for the College of Physicians and Surgeons of Saskatchewan and examiner in clinical surgery for the Dominion Council at Winnipeg, and invigilator at Saskatoon for examinations of the Royal College of Physicians and Surgeons of Canada.

Andrew Croll's interests were not confined to his profession. He was an active Mason and a leading figure in the St. Andrew's Society, the Humane Society, the St. John Ambulance, and the Cancer Society. He was a formidable opponent on the golf course and an outstanding raconteur of Scottish jokes.

He leaves a daughter and a son, Dr. L. Duncan Croll, who is an orthopaedic surgeon.

R. S. WALSH, B.M., B.Ch., F.F.A. R.C.S., D.A.

Dr. R. S. Walsh, consultant anaesthetist to the Royal Dental Hospital, died in London on November 18, aged 34.

Rodney Stephen Walsh was born on March 23, 1927, the son of the late Dr. Vincent Walsh. Educated at Sherborne and New College, Oxford, he went on to St. George's Hospital with an exhibition. Graduating B.M., B.Ch. in 1950, he held various house appointments at St. George's, the post of resident anaesthetist at the Middlesex Hospital, and later registrar at St. George's. Eventually he became senior registrar in anaesthetics jointly at St. George's and at the Southampton group of hospitals. He had recently been appointed consultant anaesthetist to the Royal Dental Hospital. He took the D.A. in 1955 and the F.F.A. R.C.S. in the following year.

Dr. Walsh was a man of exceptional ability. He had this year won the registrar's prize offered by the Section of Anaesthetics of the Royal Society of Medicine. He was keenly interested in the care of paralysed patients and in anaesthesia for dental extraction, on which he had published a book. He was considered to have a brilliant career ahead of him, and his sudden death is the more tragic because he was on its threshold.

W. FERGUSON MACKENZIE, M.B., Ch.B. F.R.F.P.S., F.D.S. R.C.S.Ed., L.D.S.

Dr. W. Ferguson MacKenzie, dental consultant to the Western Infirmary, Glasgow, died on December 12 at the age of 79.

J. C. writes: Dr. W. Ferguson MacKenzie was a man of great character who would have made his mark in any calling. He chose dentistry. Obtaining the L.D.S. in 1905, he went on to graduate M.B., Ch.B. at Glasgow University in 1906. He was a research student in the embryological section of the university from 1909 to 1912, and he was promoted to visiting dental surgeon to the Glasgow Dental Hospital in 1910. Becoming attached to the R.A.M.C. in 1911, he maintained connexion with that body until 1935, when he retired with the rank of brevet colonel. During the first world war he served with distinction on the Western Front and at the Dardanelles. Returning to his busy West End practice in Glasgow, he was invited to take up his teaching post with the Dental School. He became lecturer in dental histology in 1925 and later lecturer in dental anatomy. About the same time he was appointed dental consultant to the Western Infirmary, Glasgow, which post he held until 1952.

He became a Fellow of the Royal Faculty of Physicians and Surgeons, Glasgow, in 1910, and had the distinction of being the senior Fellow (in years) of the Faculty. He was examiner to the Faculty in the L.D.S. and H.D.D. examinations. In 1951 he was awarded the Fellowship in Dental Surgery of the Royal College of Surgeons, Edinburgh. In his earlier days he was professor in zoology in Anderson's College Medical School. It might interest his colleagues to learn that he was actually appointed professor in dental surgery and director of dental studies of Cairo University, but saw fit to decline the post. He was president of the West of Scotland Branch of the British Dental Association in 1937–8, and president of the Glasgow Odontological Society in 1934–5, as well as one of the founder members.

"Fergie Mac," as he was affectionately called by two generations of students, retained to the end his slim grace and good-humoured philosophy: he had an anecdote suited to any occasion. Until recently he seemed a permanent part of the dental scene in Glasgow. He had more than a smattering of Victorian elegance: at a testimonial dinner given in his honour some years ago those who attended acknowledged this side of his character by donning high collars and cravats. He was a gentleman in the true sense of the term; I think that this is how he would like to be remembered.

T. H. G. SHORE, M.D., F.R.C.P.

The obituary of Dr. T. H. G. Shore was published in the *Journal* of December 2 (p. 1504).

Mr. D. S. PRACY writes: In the obituary notice of T. H. G Shore there are one or two omissions of some substance. The late Professor L. R. Shore, who was professor of anatomy at Hong Kong, and during the Japanese occupation was one of those to suffer, was his younger brother. The late Dr. L. E. Shore, lecturer in physiology at Cambridge, was his uncle. During the first world war Dr. T. H. G. Shore was on the staff of No. 24 General Hospital at Étaples and was in charge of the post-mortem room and laboratory for the whole base, and many thousand post-mortem examinations were made there. Sir John Rose Bradford and Sir Hamilton Ballance, the medical and surgical consultants for the area, visited the rooms every day and discussed the findings with Shore and anyone else present. From the vast amount of material thus available many specimens prepared in their natural colour were forwarded to the Royal College of Surgeons for the war collection. Shore evolved a special technique in preparing the dry bone specimens, leaving them absolutely white.

Medical Notes in Parliament

THE SECOND OLDEST PROFESSION DEBATE ON ADVERTISING

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The House of Commons had its attention directed again on December 15 to that favourite Opposition topic among debates originated by back-benchers, the use and abuse of advertising—an occupation described by Mr. MAURICE EDELMAN during the debate as "probably the world's second oldest profession." This time the Government was asked, in a motion by Mr. E. J. MILNE (Blyth, Lab.) to note the increasing power of the advertising industry, its influence on the national life, and its effect on the economy, and to institute an independent inquiry to consider whether safeguards are necessary in the interests of the consumer public.

Three Committees at Work

The debate ended at no decisive point, since there was no division, and there will be no inquiry. The Government

spokesman, Mr. NIALL MACPHERSON, Parliamentary Secretary to the Board of Trade, was more than usually well armed in advising against it, since there are already three committees at work on one or other aspect. Much more strongly than hitherto the charge was made against advertising interests as being "the paymaster of the Press," to use Mr. Macpherson's phrase, with power to influence editorial policy. He said that he knew of no evidence of this, but in any case it was well within the scope of the Royal Commission inquiring into the economic and financial factors affecting newspaper and periodical production. Similarly, Mr. Macpherson pointed out, the Pilkington Committee was investigating all aspects of broadcasting, and was bound to be concerned with what was the main source of revenue for the independent television companies. Thirdly, the Molony Committee on consumer protection was bound to consider the descriptions applied to goods, whether by advertisers or at the point of sale, and the whole question of protecting the consumer against false claims and descriptions was open to review by it. In these circumstances it would not make sense to start another independent inquiry to cover virtually the same ground.

Advertising of Alcohol

Mr. MILNE numbered among the harmful effects of advertising which was part of his case for an inquiry the concentration by advertisers of alcohol on the very young, and the letter recently sent by the Guinness firm to several thousand doctors inviting "in strict confidence, their experience of Guinness under present-day conditions," and adding, "Should you wish to try Guinness, either for yourself or for a patient, we would be glad to send one dozen bottles free of all charges." On the economic effects of advertising he named aspirins available at a well-known chemists at 25 for 4d., in contrast with others of the same formula on sale at 27 for 1s. 8½d., and commented that as the latter were being advertised at a cost of £500,000 a year this obviously had something to do with the difference in price. Mr. WILLIAM SHEPHERD (Cheadle, Con.) added to this his knowledge of instances relating to patent medicines in which the cost of advertising was half the cost of the company's sales. He also described the practices of the Akers hair clinics, which he said had not a qualified man on the staff, although they called them trichologists, and were not even allowed to use an ultraviolet lamp under L.C.C. regulations.

Attacks on Professional Virtue

Mr. M. EDELMAN (Coventry, North, Con.) expressed the opinion that the Guinness letter to doctors was couched in rather presumptuous terms, the presumption being that the doctor had the right either to endorse its virtues or not. One doctor friend of his, he said, being unable to resist any free offer, now had two dozen bottles of Guinness which he would not drink because he did not like its taste. This technique of imposing a test on the public became an abuse when it reached out into an attack on the professional virtue of those charged with care of the public health. It had been stated before, in connexion with patent medicines, that in the past doctors had been assailed by golf balls, by offers of weekends in Paris, and by all sorts of "bribes" to try to encourage them to promote certain patent medicines. It was going rather far when it reached the stage that the manufacturers of alcoholic beverages started importuning doctors to encourage them to advocate the sale of alcohol.

Safeguards in Drug Advertising

Mr. MACPHERSON resorted to medicaments to illustrate what he had to say about existing safeguards. There were two classes of medicaments, which he described as the ethical proprietaries and those proprietaries advertised to the public. The former were the bulk of proprietary medicines prescribed under the Health Service. These were never advertised to the public, but only to the medical and allied professions through the technical journals. The main object was to reduce the danger of self-medication. In the case of proprietaries advertised to the public, there were some prohibitions: the Pharmacy and Medicines Act, 1941, prohibited the advertisement of remedies for the treatment of a number of diseases; the Cancer Act, 1939, prohibited those for cancer; and the Venereal Diseases Act, 1917, prohibited those relating to venereal disease. There was still left a wide field for public advertising, and the manufacturers, newspaper and periodical, and advertising interests had subscribed to a voluntary code of standards by which they could regulate advertisements outside the statutory limitations. This code listed 60 conditions, and in addition set out the general principles which should be followed in advertising medicines. Its observance already eliminated all but the occasional unsuitable advertisement.

In general, it was better to allow the advertising profession to control itself, and he indicated that the interests concerned were contemplating the formation of an autonomous body, to be known as the Advertising Standards Authority, which is apparently to have an independent chairman and to include independent members. The Government would certainly welcome and encourage the development of machinery for self-discipline in the advertising industry, for that they thought was the right course to follow.

Vital Statistics

Tuberculosis in Soho

A survey[1] recently published in this journal showed that tuberculosis was more than four times as common in the catering trade in Soho as in the general population. The disease was found to be twice as common among immigrants as among those born in Great Britain, and the Chinese, coming mainly from Hong Kong, had by far the highest incidence of active disease. The medical officer of health of Westminster, Dr. J. H. Briscoe-Smith, recently reported to his council the action he and the public health committee had taken to reduce the numbers of tuberculosis patients in Soho catering establishments. The public health inspectors now inquire whether cooks, waiters, and so on are *x*-rayed before engagement and advise on how *x*-ray examinations can be arranged. The Chinese Restaurateurs Association has asked all its members to see that every member of their staffs is *x*-rayed immediately. Further, announcements have been inserted in Hong Kong newspapers urging that all those seeking employment in the catering trade in Britain should be *x*-rayed before leaving. The help of the Colonial Office has been sought in putting this recommendation into effect. The Chinese Restaurateurs Association is also taking further steps to encourage those found to have tuberculosis to obtain treatment and to exclude them from work until they are certified to be non-infectious. A register of Chinese staff with details of their medical history is to be made available for inspection to officers of the Westminster public health department.

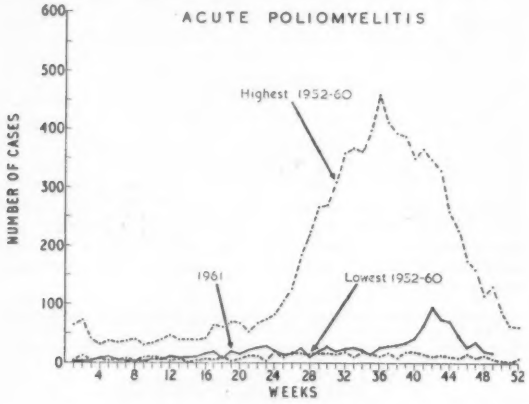
Road Casualties in October

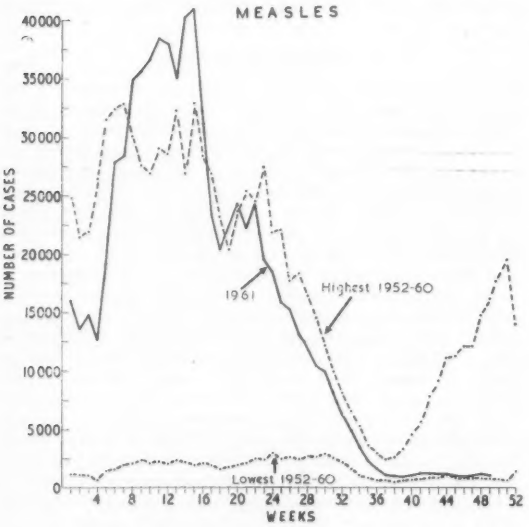
Of the 672 deaths on the roads of Britain in October 291 were pedestrians, 171 drivers or passengers in cars and other vehicles, 152 motor cyclists, scooter, or moped riders, and 58 pedal cyclists. In addition 7,872 persons were seriously injured. The total number of road deaths during the first ten months of 1961 was 5,621, an increase of 2% compared with the same period last year: fatal and serious accidents in cars increased by 10% and in goods vehicles by 8%.

[1]Emerson, P. A., Beath, Gillian, and Tomkins, J. G., *Brit. med. J.*, 1961, 2, 148

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for 1961 thus ———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending Dec. 2	Dec. 9
Dysentery		
Lincolnshire	15	17
Grimsby C.B.	10	12
Nottinghamshire	11	47
Worksop M.B.	0	44
Warwickshire	35	64
Coventry C.B.	27	55
Yorkshire West Riding	121	113
Huddersfield C.B.	53	52
Glasgow	134	115
Food Poisoning		
Suffolk	1	747
Samford R.D.	0	747

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 9** (No. 49) and corresponding week 1960.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1961 Eng. & Wales	1961 Lond.	1961 Scot.	1961 N. Ire.	1961 Eire	1960 Eng. & Wales	1960 Lond.	1960 Scot.	1960 N. Ire.	1960 Eire
Diphtheria	1	0	2	0		3	0	0	0	
Dysentery	543	24	250	15	10	563	39	142	5	5
Encephalitis, acute	1	0		0		6	1		0	
Enteric fever:										
Typhoid	0	0	0	0		1	1	0	0	
Paratyphoid	2	1	0	0		5	0	0	0	
Food-poisoning	851	6	7	2		165	23	9	0	
Infective enteritis or diarrhoea under 2 years				8	45				19	16
Measles*	1,067	39	31	50	134	7,266	499	204	49	121
Meningococcal infection	13	0	5	2		17	2	5	1	
Ophthalmia neonatorum	18	3	2	0		12	3	1	0	
Pneumonia†	273	13	176	10	1	297	15	182	1	4
Poliomyelitis, acute:										
Paralytic	13	0	0	0	1	5	3	0	0	1
Non-paralytic	4	1	0			3	0	0		
Puerperal fever§	141	31	11	3		147	23	11	1	1
Scarlet fever	480	30	33	8	9	530	17	69	19	19
Tuberculosis:										
Respiratory	316	31	64	12		415	46	76	12	
Non-respiratory	41	1	19	0		56	4	10	4	
Whooping-cough	176	7	28	3	7	1,002	81	80	11	35

DEATHS	1961 Eng. & Wales	1961 Lond.	1961 Scot.	1961 N. Ire.	1961 Eire	1960 Eng. & Wales	1960 Lond.	1960 Scot.	1960 N. Ire.	1960 Eire
Diphtheria	0	0	0	0	0	1	0	0	0	0
Dysentery	0	0		0		2	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	10	1	0	1	0	5	0	2	0	1
Influenza	45	0	0	4	2	20	0	0	0	3
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	694	48	28	23	2	554	41	23	21	12
Poliomyelitis, acute	0	0		0		0	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	65	10	8	1	3	72	3	6	3	1
Non-respiratory		0		0	0		0	0	0	0
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0–1 year	333	25	18	12	9	353	41	29	9	8
Deaths (excluding stillbirths)	11,170	852	695	140	155	10,589	872	661	155	171
LIVE BIRTHS	14,049	1227	952	220	302	14,392	1256	952	252	339
STILLBIRTHS	275	23	15			286	29	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Wellcome–Swedish Exchange Research Fellowships in Medical Science

The Wellcome Trustees have entered into an arrangement with the Medical Research Council of Sweden for the establishment of a system of exchange fellowships, under which one British research worker (or research trainee) in any branch of the natural sciences bearing upon human or animal medicine will be sent annually to work for one year at a research centre in Sweden, and one Swedish research worker or trainee within the same range of disciplines will be given comparable facilities within the United Kingdom. The cost of the scheme, which is modelled on the system of Carlsberg–Wellcome Travelling Research Fellowships established in 1957, will be shared between the Swedish Medical Research Council and the Wellcome Trust. The fellowships will include stipends ranging from £1,000 to £2,000 a year (or their equivalents in Swedish kroner) according to seniority, together with provision for travelling and certain incidental expenses. It is intended that the arrangement shall become effective at the beginning of the academic year 1962–3, and invitations to apply for these awards will be published simultaneously with the next advertisement for Carlsberg–Wellcome Travelling Research Fellows in March, 1962.

Mansel Talbot Chair of Social and Occupational Medicine, Welsh National School of Medicine

Dr. C. R. LOWE, reader in social medicine at Birmingham University since 1960, has been appointed to the Mansel Talbot chair of social and occupational medicine in the Welsh National School of Medicine from January 1.

Dr. Lowe, who was born in 1912, was educated at Dudley Grammar School and Birmingham University, qualifying M.B., Ch.B. in 1936. He took his D.P.H. in 1948 and Ph.D. in 1951. He proceeded M.D. in 1950. From 1937 to 1947 he was in general practice in Birmingham, apart from three wartime years in the R.A.M.C. in Great Britain and the Middle East. In 1948 he was appointed research scholar in the Department of Social Medicine, and from 1949 to 1960 was lecturer, first in public health and then in social medicine. He became medical adviser to the General Electric Company in 1954. In 1959 he held a Rockefeller Travelling Fellowship in the U.S.A., and has acted as consultant for W.H.O. He is a member of the Medical Research Council's Occupational Health Committee. His main researches have been in the fields of reproduction and development, morbidity and mortality, and medical services.

New Faculty of Radiology in Ireland

The President, Vice-President, and Council of the Royal College of Surgeons in Ireland have inaugurated a Faculty of Radiology. It is proposed to hold examinations for the Fellowship of the Faculty, but in the first instance the Council will award a limited number of Fellowships to Radiologists (diagnostic and therapeutic) of consultant status who have been practising radiology for not less than ten years. Persons who wish their claims to be considered should immediately send full particulars to the Registrar, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin.

Scottish National Blood Transfusion Association

The Scottish National Blood Transfusion Association was founded in 1940 and has now completed its twenty-first year. During the year ended March 31, 1961, says its annual report, the donor panel increased from 185,017 to 192,797—some 6% of the population between 18 and 65 years old. At least another 10,000 donors are needed. The five regional centres at Aberdeen, Dundee, Edinburgh, Glasgow, and Inverness collected 135,567 bottles of blood, compared with 131,358 the year before; 83,819 bottles were used as whole blood against 76,950 the previous year. The special requirements of open heart surgery (up to 20 donations of fresh compatible blood in one day for an adult) and other thoracic surgery, the increasing accident rate, and the more efficient treatment of coagulation defects are largely responsible for the rise. The anti-haemophilic fraction prepared in the Edinburgh Centre is being used in increasing amounts: 914 g. of this material was prepared.

Health Survey in City Offices

The Corporation of London is to carry out a two-year survey on the health of office and other workers in the "square mile." The object of the survey is to find out to what extent the City workers' environment is likely to comply with the requirements of legislation proposed by the Government on health, welfare, and safety in shops, offices, and other premises. The features to be investigated will include heating, lighting, ventilation, noise, overcrowding, sanitary arrangements, absentee records, sickness rates, the need for sick and accident treatment facilities, executive and other health supervision, and preventive inoculations, the supervision of toxic and dangerous practices, and co-operation with health authorities over control of food preparation and service.

Dr. ALAN ROBINSON, who is at present senior medical officer and senior specialist in hygiene at H.M. Dockyard, Portsmouth, will carry out the survey and will take up his duties on January 8. He will make an interim report at the end of the first year to the Port and City of London Health Committee and a final report a year later.

Royal Surgical Aid Society

The Royal Surgical Aid Society was founded in 1862 to provide free surgical appliances for the poor. By the time the National Health Service had made this form of charity unnecessary 1,920,210 appliances had been issued. It was then decided that the Society should devote itself to providing homes for elderly people with limited means, and two properties were acquired—one being Florence Nightingale's old home near Matlock, Derbyshire, and the other at Oxted, Surrey. These accommodate respectively 25 and 35 elderly residents of both sexes. The waiting-list grows steadily, and the Society has therefore opened a centenary fund with the hope of purchasing a third property. At least £35,000 would be needed. The Society's address is 28 Victoria Street, Westminster, London S.W.1.

British Council Annual Report

Much of the British Council's annual report for 1960–1 is devoted to the English language abroad. "It is possible," says the report, "that the literature of science and factual information may become of more importance than that of imagination and the arts in acting as a stabilising influence on the written form of English, for criteria of precision and lucidity are here most obvious and necessary for general communication. To this store of written English, which comprises an international heritage of arts and sciences, notable contributions by those who have themselves learnt English as a new language are common and likely to increase." During the year 1,146 overseas medical visitors came to the United Kingdom under the auspices of the British Council, and 68 medical tours were carried out overseas by British specialists and advisers.

University of New Zealand

From December 31 the constituent colleges of the University of New Zealand—Auckland, Victoria (Wellington), Canterbury, and Otago—will take over the powers of conferring degrees previously held by the national university.

Camden Clinic

From January 1 the British Hospital for Functional Nervous Disorders in Camden Road, London N.W.1, will be renamed the Camden Clinic.

"Family Doctor"

The January issue of *Family Doctor* is now available, price 1s. 6d. It includes articles on unwanted children, by Dr. ANN MULLINS; on bronchitis—the English disease—by Dr. J. EARLE; on earache, by Dr. K. S. HOLT; and on toxaemia of pregnancy, by Mr. ELLIOT PHILIPP.

People in the News

▶ The University of Basle has recently bestowed its honorary doctorate of medicine on Dr. WALTER PAGEL in recognition of his study of Paracelsus. Dr. Pagel was formerly consultant pathologist to the Central Middlesex Hospital, and now holds the same office at Clare Hall Hospital.

▶ Professor G. H. GREEN, assistant professor at the Postgraduate School of Obstetrics and Gynaecology, University of Auckland, has been awarded a Lederle International Fellowship for a year's study in the U.S.A.

▶ Dr. J. DUNWOODY, medical officer of Totnes District Hospital, has been selected as prospective Labour candidate for the Sutton division of Plymouth.

▶ Dr. DUNCAN MACMILLAN, physician superintendent of Mapperley Hospital, Nottingham, acted as chairman of the European Conference on the Role of the Nurse in Mental Health Practice, convened recently in Copenhagen by the Regional Office for Europe of W.H.O.

▶ Dr. P. TUTTNAUER was awarded a silver plaque for his painting "Garden, Villa Castagnola, Lugano," at the International Medical Congress's art exhibition held earlier this year in Turin.

COMING EVENTS

Moynihan Lecture.—Dr. O. H. WANGENSTEEN, "The Stomach Since the Hunters—Gastric Temperature and Peptic Ulcer," 5 p.m., January 10, Royal College of Surgeons of England, Lincoln's Inn Fields, London W.C.2.

Watson-Jones Lecture.—Mr. F. W. HOLDSWORTH, "Fractures, Dislocations, and Fracture Dislocations of the Spine," January 11, 5 p.m., Royal College of Surgeons of England, Lincoln's Inn Fields, London W.C.2.

1st International Symposium of the Manhattan Eye, Ear and Throat Hospital.—"Reconstructive and Plastic Surgery of the Eye and Adnexa," May 21–25, 1962, New York City. Details from Professor R. C. TROUTMAN, Chairman, Manhattan Eye, Ear and Throat Hospital, 210 E. 64th Street, New York 21, New York, U.S.A.

NEW ISSUES OF SPECIALIST JOURNALS

*The Journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.*1.

GUT

Long-term Medical Management and Complications of "Resistant" Ascites. William H. J. Summerskill, Bernard F. Clowdus, II, and John W. Rosevear.
Serum Haptoglobin in Liver Diseases. Roger Williams, Barbara E. Speyer, and Barbara H. Billing.
Plasma-free Fatty Acid in Liver Disease. A. Mortiaux and A. M. Dawson.
Changes in the Portal and Splenic Veins in Portal Hypertension and their Relation to Splenomegaly. John B. Wilson.
Radiological Investigation of the Small Intestine. W. G. Scott-Harden, H. A. R. Hamilton, and S. McCall Smith.
The Intestinal Absorption Defect in Cystinuria. M. D. Milne, A. M. Asatoor, K. D. G. Edwards, and Lavinia W. Loughridge.
The Effect of Corticotrophin and Corticosteroids on the External Secretion of the Pancreas in Dogs. Wilfred Sircus.
Light- and Electron-microscope Studies of the Effects of 4-aminopteroylglutamic Acid (Aminopterin) on the Mucous Membrane of the Small Intestine of the Rat. A. Wynn Williams.
Secretion of Blood Group Substances in Duodenal, Gastric and Stomal Ulcer, Gastric Carcinoma, and Diabetes Mellitus. R. Doll, H. Drane, and A. C. Newell.
Experiences with Extraperitoneal Colostomy and Ileostomy. A. Elliot-Smith and Neil S. Painter.
The Incidence and Pattern of Peptic Ulcer in Indians and Africans in Durban. A. E. Kark.
The First Recorded Case of Whipple's Disease? A. D. Morgan.
An Evaluation of Unabsorbable Markers in the Study of Fat Absorption. H. S. Wiggins and A. M. Dawson.
Gastroenterological Society of Australia: Third Annual General Meeting.

Volume 2, No. 4. (Quarterly; £3 annually.)

BRITISH JOURNAL OF OPHTHALMOLOGY

Ocular Lesions of Onchocerciasis. F. H. Budden.
Attention and Amblyopia—An Electro-encephalographic Approach to an Ophthalmological Problem. A. T. M. van Balen and H. B. Henkes.
An Operation for the Treatment of Severe Contraction of the Socket. B. W. Rycroft.
Corticosteroids and Fibrolysin in the Prevention of Lacrimal Duct Obstruction. Y. Dayal.
Nodular Dystrophy of the Trabecular Meshwork. J. S. Speakman.
Primary Malignant Melanoma of the Cornea. H. B. Stallard.
Cystic Lymphangioma of the Orbit. A. Mortada.
Unilocular Aplasia of the Optic Nerve. F. Somerville.
Laurence-Moon-Biedl Syndrome. K. S. Mehra, R. B. L. Gupta, and Y. Dayal.
Medullo-epithelioma. B. A. Sayed, K. N. Sahgal, and V. K. Desai.
Correspondence.
Reviews.
Notes.

Volume 46, No. 1. (Monthly; £6 annually. With *Ophthalmic Literature* and Index, £9.)

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Wednesday, January 3

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann and Dr. A. A. Osborn: Clinical Pathological Conference.

Thursday, January 4

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arris and Gale Lecture by Mr. D. Annis: A Study of the Regenerative Capacity of the Epithelial Lining of the Urinary Bladder, together with Evidence Concerning the Function of the Mucosa in the Reflex Act of Micturition.

Friday, January 5

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—(1) 3.30 p.m., Mr. William McKenzie: Treatment of Acute Inflammation in the Ear; (2) 5.30 p.m., Mr. N. Asherson: Some Uncommon Diseases of Childhood.

INSTITUTION OF ELECTRICAL ENGINEERS: MEDICAL ELECTRONICS DISCUSSION GROUP, Savoy Place, London W.C.—6 p.m., Dr. H. Davson, D.Sc.: Discussion on Membranes.

Saturday, January 6

MIDLAND THORACIC SOCIETY.—At 36 Harborne Road, Edgbaston, 3 p.m., short papers. Dr. A. O. Bech: Hard Metal Pneumoconiosis; Dr. M. Hemming: Spontaneous Pneumothorax; Dr. B. T. Davis: Amyloid Goitre.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Barrett.—On December 11, 1961, Arthur Max Barrett, M.D., of 183 Hills Road, Cambridge, aged 52.

Bevers.—On December 13, 1961, Edmund Cecil Bevers, C.B.E., M.B., F.R.C.S., of 39 Belsyre Court, Oxford.

Body.—On December 7, 1961, Thomas Howard Body, M.R.C.S., L.R.C.P., of Petersgate, Tenterden, Kent.

Brodie.—On December 17, 1961, at 10 Church Hill, Edinburgh, Peter Martin Brodie, M.B., F.R.C.S.Ed.

Dobbie.—On December 12, 1961, in a car accident, Edith Dennistoun Dobbie (Mrs. N. B. Rintoul), M.B., Ch.B., D.P.H., of 49 Peel Street, Partick, Glasgow.

Edwards.—On December 9, 1961, Henry Herbert Johnson Edwards, L.S.A., of 9 Cricketfield Road, Horsham, Sussex, aged 96.

Haynes.—On December 9, 1961, at Virginia House, Vinters Road, Maidstone, Kent, George Secretan Haynes, M.D., F.R.C.P., late of Corner House, Cambridge, aged 89.

Henderson.—On December 10, 1961, Alan Ashton Henderson, M.R.C.S., L.R.C.P., formerly of Golders Green, London N.W.

Laird.—On December 11, 1961, Andrew John Laird, M.D., D.P.H., of 10 Park Terrace, Nottingham, Formery of Cambridge, aged 89.

Mackenzie.—On December 12, 1961, at Glasgow, William Ferguson Mackenzie, T.D., M.B., Ch.B., F.R.F.P.S., F.D.S. R.C.S.Ed., of 9 Somerset Place, Glasgow.

Miller.—On December 11, 1961, at 54 Brisbane Street, Greenock, Renfrewshire, John Miller, M.B., Ch.B., M.R.C.O.G.

Moul.—On December 6, 1961, Samuel William Henry Moul, M.R.C.S., L.R.C.P., of Putney, London S.W.

Small.—On December 13, 1961, at his home, 23 Telegraph Lane West, Norwich, Norfolk, James Alexander Small, M.B., B.Ch., late of Heigham Hall, Norwich.

Smith.—On December 6, 1961, Stanley Wood Smith, M.B., B.S., D.P.H., Major, R.A.M.C., retired.

Thompson.—On December 10, 1961, James Gibb Thomson, M.B., Ch.B., of Coombe Hill House, Radstock, Bath, Som.

Warner.—On December 11, 1961, at St. George's Hospital, Tooting Grove, London S.W., Antony Rhys Warner, M.B., B.S., M.R.C.P., D.Obst.R.C.O.G.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Cervical Erosions

Q.—*Would it be satisfactory treatment to cauterize cervical erosions with a silver nitrate stick or trichloracetic acid in general practice in the surgery without anaesthesia?*

A.—Chemical cauterization of cervical erosions is not satisfactory treatment because any infection is too deep to be cured by such surface therapy. The good results of such treatment of postnatal erosions might seem to contradict this, but such erosions have such a high rate of spontaneous cure within six months of delivery that they should be left untreated until the end of that time. Not only chemical but also the preferred linear electric cauterization can be performed without anaesthesia in most women. Treatment of any cervical erosion or infection should be preceded by the taking of a cytology smear in all cases and by biopsy in some to exclude premalignant and malignant change.

Variations in Immunization Schedules

Q.—*In the recent Ministry of Health immunization schedules (P and Q)[1] it is advised that children should be given diphtheria and tetanus immunization at school entry and again between 8 and 12 years of age. There are many children in these age groups who have had a primary course of immunization against diphtheria but who have not previously received any form of tetanus immunization. What is the best routine pattern for the immunization of these children?*

A.—When a child of 5 to 12 years who has been immunized in infancy only against diphtheria is presented for simultaneous reinforcement of immunity to diphtheria and primary immunization against tetanus the following schedule should be used:

(1) Tetanus toxoid (Tet/Vac).
Interval of 4 to 6 weeks.
(2) Diphtheria and tetanus vaccine (DT/Vac).
Interval of 4 to 6 weeks.
(3) Tet/Vac or DT/Vac.

The first injection should be Tet/Vac alone, because if DT/Vac were given there would be a danger that the response to the diphtheria component would be so marked (because of the primary immunization in infancy) that the response to the tetanus component would be insignificant. If the primary immunization against diphtheria in infancy was thorough (and particularly if alum-containing vaccines were used) the third injection of the schedule should be tetanus toxoid. If, however, the primary course was incomplete (e.g., two instead of three doses of the relatively weaker antigens F.T. or T.A.F.) the third injection should be DT/Vac.

It should be remembered that the older the child the greater is the possibility of a reaction to diphtheria vaccine. After the age of 8 to 10 years it is desirable (though admittedly not always practicable) to do a preliminary Schick test in order to pick out the "pseudo" reactors, who are the subjects most likely to have a severe reaction to the vaccine. They are almost always immune to diphtheria and in no need of a reinforcing dose of vaccine.

In the above schedule the intervals between the doses of tetanus toxoid are not optimal but they are convenient. Because the response may not be maximal a reinforcing dose should be given at the first convenient opportunity and certainly before five years have elapsed. If the schedule is used at school entry this fourth dose may be given in the form of DT/Vac at 8 to 10 years (schedules B,[2] P, and Q). If, however, it is used in the 8 to 12 years period tetanus reinforcement would be desirable two to three years later—possibly about the time that B.C.G. is given.

REFERENCES

1 *Brit. med. J.*, 1961, 2, 763.
2 *Proceedings of a Symposium on Immunization in Childhood*. 1960. E. and S. Livingstone, Edinburgh. See also *Brit. med. J.*, 1959, 1, 1342.

Pregnancy and Disseminated Sclerosis

Q.—*What effect is a pregnancy likely to have in a girl in her early twenties who suffers from mild but quite definite disseminated sclerosis?*

A.—The old view that pregnancy caused a deterioration in the condition of disseminated (multiple) sclerosis is no longer accepted. This disease is characterized by phases of exacerbation with intervening apparently non-progressive phases. Although exacerbations may occur either during or after pregnancy they are no more frequent or severe than they are in women of similar age who do not become pregnant.[1 2 3] Nor does disseminated sclerosis usually interfere in any way with the normal progress of pregnancy and labour. Thus if the patient in question conceives the pregnancy and labour should be managed in the usual way and the disseminated sclerosis treated as it would be in the absence of pregnancy.

It may be added that in advanced cases of disseminated sclerosis with severe mental or physical disability pregnancy may create mechanical problems and the woman may be incapable of caring for the child after birth. Only in such special circumstances do the questions of therapeutic abortion and sterilization seriously arise.

REFERENCES

1 Tillman, A. J. B., in *Multiple Sclerosis and the Demyelinating Diseases*. 1950. The Williams and Wilkins Co., Baltimore.
2 Sweeney, W. J., *Amer. J Obstet. Gynec.*, 1953, 66, 124.
3 McAlpine, D., Compston, N. D., and Lumsden, C. E., *Multiple Sclerosis*. 1955. The Williams & Wilkins Co., Baltimore; Livingstone, Edinburgh.

Normal Pregnancy After Threatened Abortion

Q.—*If depot injections of hydroxyprogesterone capronate are successful in preventing a threatened abortion, is there a risk that an abnormal pregnancy will be made to continue to term?*

A.—When abortion is threatened it is extremely doubtful whether the giving of progestogens influences the outcome. At least their value has never been established by controlled observations. There is always a 70% chance that the pregnancy will continue without treatment, and when it does not this is generally because the foetus is already dead or abnormal.[1] When a pregnancy survives the threat of abortion the evidence suggests that the chance of a malformed child being born is not increased, nor is there a greater likelihood of placenta praevia, abruptio placentae, or premature labour, although the last is disputed.[2 3 4] In other words, the very fact that a pregnancy survives the disturbance, with or without hormone therapy, is a sign that the foetus is not malformed or harmed. The chance of a normal healthy child resulting in such circumstances is said to be 98%.

Another argument against the administration of progestogens for threatened or recurrent abortion is that they themselves can cause foetal malformation—namely, virilization of the female foetus. At least, this happens in certain women. But progestogens vary in their androgenic effect, and the one mentioned—namely, hydroxyprogesterone capronate—is relatively safe from this standpoint.[5 6]

REFERENCES

1 Colvin, E. D., in *Progress in Gynecology*, Vol. 2, 1950, edited by J. V. Meigs and S. H Sturgis. Grune and Stratton, New York; Heinemann, London.
2 —— Bartnolomew, R. A., Grimes, W. H., and Fish, J. S., *Amer. J. Obstet. Gynec.*, 1950, 59, 1208.
3 Burge, E. S., ibid., 1951, 61 615.
4 King, A. G., *Obstet. and Gynec.*, 1953, 1, 104.
5 *Brit. med. J.*, 1960, 2, 723.
6 Ibid., 1961, 2, 1205.

Peroneal Muscular Atrophy

Q.—*Is there any treatment for peroneal muscular atrophy (Charcot–Marie–Tooth type)? The patient is a young man, aged 30, with marked wasting of both legs from mid-thigh downwards.*

A.—Peroneal muscular atrophy (Charcot–Marie–Tooth type) is a familial condition in which the muscle wasting and weakness is caused by a degeneration in the relevant peripheral nerves. No treatment is known which influences the course of the disease. It is most unusual for wasting to extend above the middle of the thighs or in the arms above the elbows, and the actual disability is frequently much less than one might expect when looking at the marked peripheral wasting.

Prognosis in von Willebrand's Disease

Q.—*Two young girls have been diagnosed as having von Willebrand's disease. What effect is this likely to have on menstruation and childbirth? Is there any treatment?*

A.—Von Willebrand's disease is a bleeding tendency inherited as a simple dominant associated with variable laboratory findings, the commonest being a long bleeding-time, positive tourniquet test, and a low plasma level of antihaemophilic globulin (Factor VIII). Clinically the disease varies very considerably in severity. The most mildly affected patients have little trouble from bleeding except after dental extraction or tonsillectomy, and in these events bleeding is usually controlled by pressure. At the other extreme bleeding from epistaxis and menorrhagia may be so severe as to endanger life from the amount of blood lost at each episode. The prognosis, therefore, varies much from case to case. The commonest forms of bleeding in the severely affected patients are epistaxis, menorrhagia, bruising, gastrointestinal bleeding, and immediate bleeding from trauma. There is no corrective treatment for the condition, and the more severely affected patients should be under the supervision of a specialist centre for the care of patients with haemorrhagic states.

Grades of Milk

Q.—*What are the various grades of milk available in this country, and what percentage of cream do they contain? Does pasteurization abolish the risk of brucellosis?*

A.—The following are the official designations of milk available in England and Wales: tuberculin-tested farm-bottled; tuberculin-tested pasteurized; pasteurized; and sterilized. In addition, homogenized milk is available in some areas. These milks are required to have a fat content of not less than 3%, and will normally contain at the lowest 3.3–3.5% fat during the months of May and June and up to about 3.8% in October and November.

Milk from Channel Islands and South Devon cows may be sold separately and at a higher price. If this is done the milk must contain not less than 4% butter fat and will normally be of the order of 4.3–4.8% fat.

Pasteurization as defined in the Milk (Special Designations) Regulations, 1960, should ensure the destruction of the organisms responsible for brucellosis.

U.V.L. for Psoriasis

Q.—*Which of the comparatively inexpensive ultra-violet lamps on the market would be most suitable for the home treatment of chronic psoriasis? What dosage would you recommend?*

A.—The cheapest effective lamp costs £25 to £30, and this is the guide to suitability for treatment of psoriasis. Treatment should be taken daily after the toilet bath and should be in near-erythema dosage. With such a lamp this means starting at about a half-minute exposure, at a distance of three feet (0.9 m.) from the burner, and slowly increasing. Dosage beyond three minutes should not be necessary and becomes a burden.

NOTES AND COMMENTS

Ephedrine in Heart Block.—Dr. P. J. HORSEY (Southampton) writes: I was interested to see in your issue of November 4 ("Notes and Comments" p. 1238; see also "Any Questions?" October 7, p. 971) that your expert says that isoprenaline should be given with care intravenously. I have been trying unsuccessfully to obtain a parenteral preparation of isoprenaline which could be used intravenously, and would be most grateful for any information which your expert can give me. What sort of doses does he recommend and what dilution and rate of injection does he consider to be safe?

OUR EXPERT replies: In answer to the question on intravenous isoprenaline; this is made up in a strength of 0.02 mg. in 2 ml. of water for injection with sodium metabisulphite as a stabilizer. 2 ml. may be given in an adult but a proportionately smaller dosage is used in children. Suppositories are made up in the strength of 2.5 to 5 mg. The intravenous preparation need not be further diluted or injected particularly slowly.

Lowering Blood Cholesterol.—Dr. A. JORDAN (Department of Chemical Pathology, The Royal Hospital, Sheffield) writes: The reply in "Any Questions?" (November 4, p. 1237) under this heading can lead to misconceptions. Does the reply relate to whole-blood cholesterol (not much used nowadays) or to serum cholesterol? The method of determination needs to be stated: results obtained by applying the Liebermann–Burchardt reaction to an extract without hydrolysis of the cholesterol esters gives results about 5–25% higher than true cholesterol values when the free : ester cholesterol ratio is normal. Results are also affected by the method of extraction used. The reply given seems to regard a "blood cholesterol" of 348 mg./100 ml. as high; if this be a serum cholesterol the result is either within normal limits or is raised, depending upon the method of determination used.

OUR EXPERT replies: In answering the question it was assumed that the blood cholesterol referred to plasma cholesterol, and I interpreted the result in terms of the method of estimation with which I am familiar, that of Zak and Zlatkis. With this method hydrolysis of the cholesterol esters is irrelevant, as the result is the same with or without hydrolysis. The level of 348 mg.% is definitely above the upper 1%[1] level for this method, which is 324 mg.%. It therefore seems reasonable to interpret the level of 348 mg.% as indicating hypercholesterolaemia, and most clinicians would probably agree with this interpretation. It would probably have been wise, as Dr. Jordan implies, to have asked the questioner what method was used for estimating the cholesterol in this patient, and I am grateful to Dr. Jordan for pointing out the importance of mentioning the method of estimation used in a test with such wide limits of normality.

REFERENCE

[1] King, E. J., and Wooton, I. D. P., *Micro-analysis in Medical Biochemistry*, 3rd ed., 1956. Churchill, London.

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